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Constraint-Induced Movement Therapy for Rehabilitation of Arm Dysfunction After Stroke in Adults: An Evidence-Based Analysis

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Effective April 5, 2011, the Medical Advisory Secretariat (MAS) became a part of Health Quality Ontario (HQO), an independent body funded by the Ministry of Health and Long-Term Care. The mandate of the Medical Advisory Secretariat is to provide evidence-based recommendations on the coordinated uptake of health services and health technologies in Ontario to the Ministry of Health and Long-Term Care and to the health care system. This mandate helps to ensure that residents of Ontario have access to the best available and most appropriate health services and technologies to improve patient outcomes.

To fulfill its mandate, the Medical Advisory Secretariat conducts systematic reviews of evidence and consults with experts in the health care services community. The resulting evidence-based analyses are reviewed by the Ontario Health Technology Advisory Committee—to which MAS also provides a secretariat function—and published in the *Ontario Health Technology Assessment Series.*

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To conduct its comprehensive analyses, the Medical Advisory Secretariat systematically reviews the available scientific literature, making every effort to consider all relevant national and international research; collaborates with partners across relevant government branches; consults with clinical and other external experts and developers of new health technologies; and solicits any necessary supplemental information.

In addition, the Secretariat collects and analyzes information about how a new technology fits within current practice and existing treatment alternatives. Details about the technology's diffusion into current health care practices add an important dimension to the review of the provision and delivery of the health technology in Ontario. Information concerning the health benefits; economic and human resources; and ethical, regulatory, social and legal issues relating to the technology assist decision-makers in making timely and relevant decisions to optimize patient outcomes.

The public consultation process is available to individuals wishing to comment on an analysis prior to publication. For more information, please visit http://www.health.gov.on.ca/english/providers/program/ohtac/public_engage_overview.html.

Disclaimer

This evidence-based analysis was prepared by the Medical Advisory Secretariat for the Ontario Health Technology Advisory Committee and developed from analysis, interpretation, and comparison of scientific research and/or technology assessments conducted by other organizations. It also incorporates, when available, Ontario data and information provided by experts and applicants to the Medical Advisory Secretariat to inform the analysis. While every effort has been made to reflect all scientific research available, this document may not fully do so. Additionally, other relevant scientific findings may have been reported since completion of the review. This evidence-based analysis is current to the date of the literature review specified in the methods section. This analysis may be superseded by an updated publication on the same topic. Please check the Medical Advisory Secretariat website for a list of all evidence-based analyses: http://www.health.gov.on.ca/ohtas.

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List of Abbreviations

ADL	Activities of Daily Living
ARAT	Action Research Arm Test
AOU	Amount of Use
BI	Barthel Index
CI	Confidence interval(s)
CIMT	Constraint-Induced Movement Therapy
FIM	Functional Independence Measure
FMA	Fugl-Meyer Motor Assessment
FU	Forced Use Therapy
IADL	Instrumental Activities of Daily Living
ICER	Incremental Cost-Effectiveness Ratio
MAL	Motor Activity Log
mCIMT	Modified Constraint-Induced Movement Therapy
MD	Mean Difference
n	Sample Size
OR	Odds ratio
OHTAC	Ontario Health Technology Advisory Committee
QALY	Quality Adjusted Life Years
QOM	Quality of Movement
RCT	Randomized controlled trial
RR	Relative risk
RTT	Repetitive Task Training
SD	Standard deviation
SIS	Stroke Impact Scale
TIA	Transient Ischemic Attack
WMFT	Wolf Motor Function Test

Executive Summary

Objective

The purpose of this evidence-based analysis is to determine the effectiveness and cost of CIMT for persons with arm dysfunction after a stroke.

Clinical Need: Condition and Target Population

A stroke is a sudden loss of brain function caused by the interruption of blood flow to the brain (ischemic stroke) or the rupture of blood vessels in the brain (hemorrhagic stroke). A stroke can affect any number of areas including the ability to move, see, remember, speak, reason, and read and write. Stroke is the leading cause of adult neurological disability in Canada; 300,000 people or 1% of the population live with its effects. Up to 85% of persons experiencing a complete stroke have residual arm dysfunction which will interfere with their ability to live independently. Rehabilitation interventions are the cornerstone of care and recovery after a stroke.

Constraint-Induced Movement Therapy

Constraint-Induced Movement (CIMT) is a behavioural approach to neurorehabilitation based on the principle of 'learned non-use'. The term is derived from studies in nonhuman primates in which somatosensory deafferentation of a single forelimb was performed and after which the animal then failed to use that limb. This failure to use the limb was deemed 'learned non-use'. The major components of CIMT include: i) intense repetitive task-oriented training of the impaired limb ii) immobilization of the unimpaired arm, and iii) shaping. With regard to the first component, persons may train the affected arm for several hours a day for up to 10-15 consecutive days. With immobilization, the unaffected arm may be restrained for up to 90% of waking hours. And finally, with shaping, the difficulty of the training tasks is progressively increased as performance improves and encouraging feedback is provided immediately when small gains are achieved.

Research Question

What is the effectiveness and cost of CIMT compared with physiotherapy and/or occupational therapy rehabilitative care for the treatment of arm dysfunction after stroke in persons 18 years of age and older?

Research Methods

Literature Search

Search Strategy

A literature search was performed on January 21, 2011 using OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, OVID EMBASE, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), and the Cochrane Library, Centre for Reviews and Dissemination. (Appendix 1) A preliminary search completed in August 2010 found a Cochrane Systematic review published in 2009. As a result, the literature search for this evidence-based analysis was designed to include studies published from January 1, 2008 to January 21, 2011.

Inclusion Criteria

- Systematic reviews of randomized controlled trials with or without meta-analysis.
- Study participants 18 years of age and older with arm dysfunction after stroke.
- Studies comparing the use of CIMT with occupational therapy and/or physiotherapy rehabilitative care (usual care) to improve arm function.
- Studies which described CIMT as having the following three components: i) restraining unimpaired arm and/or wrist with a sling, hand splint or cast; ii) intensive training with functional task practice of the affected arm; iii) application of shaping methodology during training. No restriction was placed on intensity or duration of treatment otherwise.
- Duration and intensity of therapy is equal in treatment and control groups.
- Therapy beginning a minimum of one month after stroke.
- Published between 2008 and 2011.

Exclusion Criteria

- Narrative reviews, case series, case reports, controlled clinical trials.
- Letters to the editor
- Grey literature.
- Non-English language publications.

Outcomes of Interest

Primary Outcome

- Arm motor function: Action Research Arm Test (ARAT)

Secondary Outcome

- Arm motor impairment: Fugl-Meyer Motor Assessment (FMA)
- Activities of daily living (ADL): Functional Independence Measure (FIM), Chedoke Arm and Hand Inventory
- Perceived motor function: Motor Activity Log (MAL) Amount of Use (AOU) and Quality of Movement (QOM) scales
- Quality of Life: Stroke Impact Scale (SIS)

Summary of Findings

A significant difference was found in our primary outcome of arm motor function measured with the Action Research Arm Test in favour of CIMT compared with usual care delivered with the same intensity and duration. Significant differences were also found in three of the five secondary outcome measures including Arm Motor Impairment and Perceived Motor Function Amount of Use and Quality of Use. There was a nonsignificant effect found with the FIM score and the quality of life Stroke Impact Scale outcome measure. The nonsignificant effect found with the scale score and the quality of life score may be a factor of a nonresponsive outcome measure (FIM scale) and/or a type II statistical error from an inadequate sample size. The quality of evidence was moderate for arm motor function and low for all other outcome measures except quality of life, which was very low.

Table 1: Summary of Results*

Outcome	Outcome Measure	Number of Studies (n)	Mean Difference in Change scores CIMT vs. Usual Care [95% C.I.]	Results	GRADE Quality of Evidence
Arm motor function	Action Research Arm Test	4 (43)	13.6 [8.7, 18.6]	Significant	Moderate
Arm motor impairment	Fugl-Meyer Motor Assessment	8 (169)	6.5 [2.3, 10.7]	Significant	Low
Activities of daily living	Functional Independence Measure	4 (128)	3.6 [-0.22, 7.4]	Nonsignificant	Low
Self-reported amount of arm use	Perceived Arm Motor Function (Amount of Use) Scale	8 (241)	1.1 [0.60, 1.7]	Significant	Low
Self-reported quality of arm use	Perceived Arm Motor Function (Quality of Use) Scale	8 (241)	0.97 [0.7, 1.3]	Significant	Low
Quality of life	Stroke Impact Scale	2 (66)	3.9 [-5.6, 13.5]	Nonsignificant	Very Low

*CI, Confidence Intervals; n, Sample Size

Background

Objective of Analysis

The purpose of this evidence-based analysis is to determine the effectiveness and cost of Constraint-Induced Movement Therapy (CIMT) for persons with arm dysfunction after a stroke.

Clinical Need and Target Population

Description of Problem

A stroke is a sudden loss of brain function caused by the interruption of blood flow to the brain (ischemic stroke) or the rupture of blood vessels in the brain (hemorrhagic stroke). A stroke can affect any number of functions, including the ability to move, see, remember, speak, reason, and read and write. (1) About 80% of strokes are ischemic. About 20% of strokes are hemorrhagic, which means they are caused by uncontrolled bleeding in the brain. A Transient Ischemic Attack (TIA), also known as a "mini-stroke," is caused by a temporary interruption of blood flow to the brain. A TIA is an important warning sign that puts persons at increased risk of a complete stroke. (1)

Stroke is the leading cause of adult neurological disability in Canada, with 300,000 people or 1% of the population living with its effects. (2) Up to 85% of persons experiencing a complete stroke may have residual arm dysfunction which will interfere with their ability to live independently. (3) Rehabilitation interventions are the cornerstones of care and recovery after stroke.

Ontario Prevalence and Incidence

There were 19,395 persons with stroke (this includes intracerebral hemorrhage, ischemic stroke, subarachnoid hemorrhage, and transient ischemic attack) presenting to emergency departments in 2007/2008, with 15,514 admitted to the hospital. (4)

Rehabilitation

According to the 2010 Institute of Clinical Evaluative Sciences Ontario Stroke Evaluation Report, (4) the mean number of rehabilitation services offered by Community Care Access Centres) to patients discharged from hospital in 2006/2007 after an acute stroke episode was 4 visits for physical therapy, 3 for occupational therapy, and 3 for speech-language pathology. Furthermore, the CCAC service intensity was found to be low and likely inadequate in terms of helping to bring about functional changes in those who had difficulty living independently. Finally, no existing database collects information on outpatient therapy offered in ambulatory settings at hospitals and clinics in Ontario. This Stroke Evaluation Report recommended the following:

1. Survey outpatient facilities to identify those providing therapies of benefit to stroke patients.
2. The National Ambulatory Care Reporting System database maintained by the Canadian Institute for Health Information needs to evolve to capture ambulatory rehabilitation being delivered at inpatient facilities (both acute and rehabilitative).
3. Investment in CCAC rehabilitation services could potentially reduce rates of readmission to hospitals and admission to long-term care institutions.

Overall, the Report concluded that people with stroke living in the community who have difficulty with activities of daily living should have access, as appropriate, to therapy services to improve or prevent deterioration in these activities.

It is generally agreed that the target FIM® score for admission to stroke rehabilitation is 40 to 80. A provincial median admission FIM® score of 78 (average score, 76) suggests that a notable proportion of patients in the severe group (those with an FIM® score of less than 60) did not have access to inpatient rehabilitation. This might also suggest that patients with mild disability were going to inpatient rehabilitation due to a lack of outpatient services and/or pressures on inpatient rehabilitation centres to reduce length of stay. (4)

Discharge Destination after Hospitalization

In their 2010 Ontario Stroke Evaluation Report, (4) the Institute of Clinical Evaluative Sciences) found that provincially, there was a 27% increase in discharging stroke patients home with services (from 11% in 2003/2004 to 14% in 2007/2008) and an associated decrease in discharging home without services (from 45% in 2003/2004 to 41% in 2007/2008). There was a slight decrease in discharging to long-term care (from 8.5% in 2003/2004 to 7% in 2007/2008) and complex continuing care (from 9% in 2003/2004 to 7% in 2007/2008) and a 15% relative increase in discharging to inpatient rehabilitation (from 20% in 2003/2004 to 23% in 2007/2008).

Persons with a modified Rankin score between 3 and 5, indicating moderate to severe stroke, are considered to be the most suitable for inpatient rehabilitation. Based on the 2004/2005 provincial stroke audit, these patients represent 36.8% of the acute stroke inpatient population. Therefore, the estimated proportion of stroke patients needing inpatient rehabilitation is 35%-40%. (4)

On average, 2 out of 10 persons admitted to hospital due to stroke were transferred to rehabilitation. There is a wide variation (14.1% to 32.2%) among Local Health Integration Networks regarding the proportion of stroke patients discharged to inpatient rehabilitation. Access to rehabilitation was much higher among designated stroke centres where 3 out of 10 patients were discharged to inpatient rehabilitation. (4)

Constraint-Induced Movement Therapy

Constraint-Induced Movement Therapy (CIMT) is a behavioural approach to neurorehabilitation based on the principle of ‘learned non-use’. The term is derived from studies of nonhuman primates in which somatosensory deafferentation of a single forelimb was performed, after which the animal then failed to use that limb. (5) The major components of CIMT include: i) intense, repetitive, task oriented training of the impaired limb; ii) immobilization of the unimpaired arm; and iii) shaping. (5;6) With regard to the first component, persons may train the affected arm for several hours a day for up to 10-15 consecutive days. With immobilization, the unaffected arm may be restrained for up to 90% of waking hours. And finally, with shaping, the difficulty of the training tasks is progressively increased as performance improves and encouraging feedback is provided immediately when small gains are achieved. (5)

Evidence-Based Analysis

Research Question

What is the effectiveness and cost of CIMT compared with physiotherapy and/or occupational therapy rehabilitative care of equal intensity and duration for the treatment of arm dysfunction in persons 18 years of age and older?

Research Methods

Literature Search

Search Strategy

A literature search was performed on January 21, 2011 using OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, OVID EMBASE, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), and the Cochrane Library, Centre for Reviews and Dissemination (Appendix 1). The literature search was designed to include studies published from January 1, 2008 to January 21, 2011 due to an existing Cochrane Systematic review on CIMT which searched the literature up to and including June 2008.

Abstracts were reviewed by one reviewer and full-text articles were obtained for studies meeting eligibility criteria. Reference lists were also examined in order to locate any additional relevant studies that were not identified through the search. Articles that did not clearly meet the eligibility criteria were reviewed with a second clinical epidemiologist and subsequently by a group of epidemiologists until consensus was established about whether the articles met the criteria.

Inclusion Criteria

Studies meeting the following criteria were included in this systematic review:

- Systematic reviews of randomized controlled trials with or without meta-analysis.
- Study participants 18 years of age and older with arm dysfunction after stroke.
- Studies comparing the use of CIMT with occupational therapy and/or physiotherapy rehabilitative care (usual care) to improve arm function.
- Studies which described CIMT as having the following three components: i) restraining unimpaired arm and/or wrist with a sling, hand splint or cast; ii) intensive training with functional task practice of the affected arm; and iii) application of shaping methodology during training.
- No restriction was placed on intensity or duration of treatment otherwise.
- Duration and intensity of therapy is equal in treatment and control groups.
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Exclusion Criteria

Studies meeting the following criteria were excluded from this systematic review:

- Narrative reviews, case series, case reports, controlled clinical trials
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Outcomes of Interest

Primary Outcome

- Arm motor function: Action Research Arm Test (ARAT)

Secondary Outcome

- Arm motor impairment: Fugl-Meyer Motor Assessment (FMA)
- Activities of daily living (ADL): Functional Independence Measure (FIM), Chedoke Arm and Hand Inventory
- Perceived motor function : Motor Activity Log (MAL) Amount of Use (AOU) and Quality of Movement (QOM) scales
- Quality of life: Stroke Impact Scale (SIS)

Description of Outcome Measures:

Action Research Arm Test (ARAT) is a 19-item test divided into 4 categories including grasp (lifting different size objects), grip (holding and moving objects), pinch (picking up small objects), and gross movement (e.g., hand to mouth actions). Each item is graded on a 4-point ordinal scale (0=can perform no part of the test; 1=performs test partially; 2=completes test but takes abnormally long time or has great difficulty; 3=performs test normally) for a total possible scale score of 57, with higher scores indicating better ability. (7) The scale has been extensively examined and used as a 'gold standard' for comparison with other upper limb measures such as the Chedoke Arm and Hand Inventory. (8)

Chedoke Arm and Hand Inventory (CAHI) is a test developed to measure functional tasks in people poststroke. It consists of 13 functional tasks that reflect domains deemed important by survivors of stroke, including bilateral activities, non-gender specific tasks, and the full range of movements, pinches, and grasps covering all stages of motor recovery poststroke. Correlation between CAHI and the ARAT was high (r=0.93). (8)

Fugl-Meyer Motor Assessment (FMA) (Upper Extremity Portion) assesses motor performance across the domains of voluntary movement, reflex activity, grasp, and coordination. Performance is measured on 33 tasks within these domains using a 3-point ordinal scale (0=cannot perform; 1=performs partially; and 2=performs fully) for a total possible scale score of 66 (3;8), with higher scores representing better performance. The reliability and construct validity of the FMA are well established.

Functional Independence Measure (FIM) is an 18-item scale grouped into 6 subscales measuring self-care, sphincter control, transfers, locomotion, communication, and social cognition. Each item is rated from 1 to 7 based on the required level of assistance necessary to perform the basic activities of daily living (ADL) (1= complete assistance needed; 2= maximal assistance; 3= moderate assistance; 4= minimal assistance; 5=supervision; 6= modified independence; and 7= complete independence) with a total possible scale score of 126. (9) A higher score indicates greater independence. (10)

Motor Activity Log (MAL) is a semi-structured self-report questionnaire designed to obtain information about the use of the affected limb during 30 minutes of important ADL. There is a 6-point Amount of Use (AOU) subscale to rate the extent to which the arm was used and a 6-point Quality of Use (QOU) subscale to rate the quality of use or how well persons are using their affected arm. (9) Each subscale consists of 20 common activities of daily living scored from 0 (never use the more affected arm for this activity) to 5 (always use the more affected arm for this activity) on the AOU subscale and from 0 (unable to use the more affected arm for this

activity) to 5 (able to use the more affected arm for this activity) on the QOU subscale. The MAL has good inter-rater reliability and construct validity. (3) The MAL is considered a primary measure of CIMT outcome. (11)

Stroke Impact Scale (SIS) is a comprehensive measure of health outcomes in stroke populations. Version 2 is a 64-item self-report scale designed to assess 8 functional domains including strength, memory, emotions, communication, ADLs, and instrumental ADL (IADL)., Instrumental ADL include activities such as housework, taking medications properly, mobility, hand function, and domestic and community participation. The SIS has established reliability and validity. Version 3 is a 59-item self-report scale designed to assess eight functional domains. These functional domains include strength, memory, emotion, communication, ADLs/IADL, mobility, and hand function. Items in each domain in both versions are scored using a 5-point rating scale. Aggregated scores in each domain are generated with a higher score indicating better performance. (12)

Statistical Analysis

Where appropriate, a meta-analysis was undertaken to determine the pooled-estimate of effect of CIMT compared with usual care for explicit outcomes using Review Manager 5 version 5.0.25. Mean difference was used as the pooled summary estimate for continuous data where the outcome among pooled studies was measured by the same scale. The degree of statistical heterogeneity among studies was assessed by the I^2 -statistic for each outcome. A fixed or random effects model was used following the guidance of the Cochrane handbook. (13) An I^2>50% was considered as substantial heterogeneity for which a subgroup analysis was undertaken. (13) A subgroup analysis was also undertaken to explain inconsistencies in study results. A subgroup analysis was performed using three categories similar to Sirtori et al. (14) including: i) program (high intensity/short duration (H/S) or low intensity/long duration (L/L); ii) position of restraint (hand or arm and hand); and, iii) time since stroke (1-12 months or more than 12 months).

Quality of Evidence

The quality of the body of evidence was assessed as high, moderate, low, or very low according to the GRADE Working Group criteria (15) as presented below.

- Quality refers to criteria such as the adequacy of allocation concealment, blinding, and losses to follow-up.
- Consistency refers to the similarity of estimates of effect across studies. If there are important and unexplained inconsistencies in the results, confidence in the estimate of effect for that outcome decreases. Differences in the direction of effect, the magnitude of the difference in effect, and the significance of the differences guide the decision about whether important inconsistency exists.
- Directness refers to the extent to which the population, interventions, and outcome measures are similar to those of interest.

As stated by the GRADE Working Group, the following definitions of quality were used in grading the quality of the evidence:

High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain.

Results of Evidence-Based Analysis

Three systematic reviews (13-15) and one randomized controlled trial (3) were obtained from the literature search (see Figure 1, and Table 1).

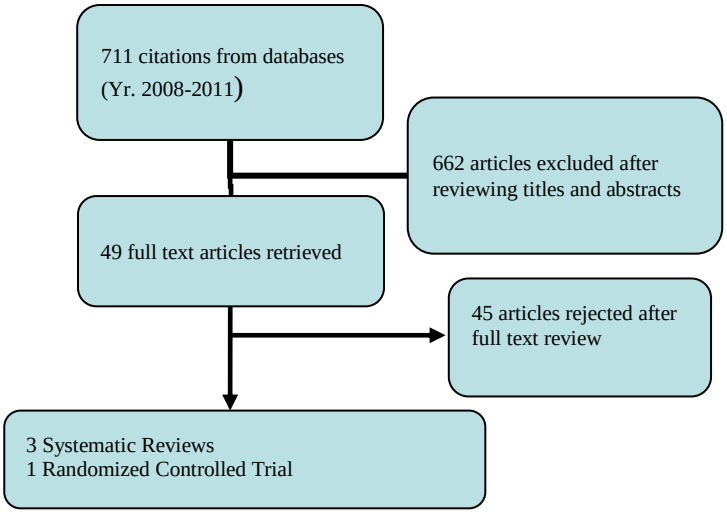

Figure 1: Literature Search

Table 1: Body of Evidence Examined According to Study Design (16)*

Study Design	Number of Eligible Studies
RCT Studies	
Systematic review of RCTs	3
Large RCT	
Small RCT	1
Observational Studies	
Systematic review of non-RCTs with contemporaneous controls	
Non-RCT with contemporaneous controls	
Systematic review of non-RCTs with historical controls	
Non-RCT with historical controls	
Database, registry, or cross-sectional study	
Case series	
Retrospective review, modelling	
Studies presented at an international conference or other sources of grey literature	
Expert opinion	
Total	4

*RCT indicates randomized controlled trial.

Characteristics of Included Studies

Systematic Reviews

Table 2 presents an overview of the characteristics of the 3 systematic reviews found during the literature search. The most recent review, published in 2010, was that completed by Corbetta et al. (17) which was an update of that done by Sirtori et al. (14) and published by the Cochrane Collaboration in 2009. Corbetta et al. (17) reported the results of CIMT compared with usual care of disability measured with the FIM and Barthel index, and motor function measured with the ARAT scale. Sirtori et al. (14) reported the results of these measures as well as the effects of CIMT on perceived arm motor impairment measured with the MAL, arm motor impairment measured with the FMA, and quality of life measured with the SIS. Both Sirtori et al. (14) and Corbetta et al. (17) pooled studies that compared Forced Use Therapy (like CIMT, this intervention involves the restraint of the non-involved upper extremity and intensive practice with the involved upper extremity) with CIMT in their meta-analysis. Forced Use Therapy does not include the intensive training and shaping components of CIMT. Therefore, because studies examining Forced Use Therapy were combined with CIMT without subgroup analyses of each, the results of these two systematic reviews are not directly applicable to the research question of this evidence-based analysis.

The systematic review by French et al. (18) searched the databases up to September 2006 and included studies of repetitive task training and treadmill training. A subgroup analysis determined a significant effect of CIMT on arm function but not on hand function (Table 2).

Table 2: Characteristics of Systematic Reviews of CIMT for Upper Limb Dysfunction in Adult Stroke Patients*

Author, Year	Purpose of Review	Search date	Population	Total No. of Studies	Meta-analysis	Conclusion
Corbetta et al, 2010 (17)	The effectiveness of CIMT, modified CIMT, FU compared with other techniques, or no treatment in adult stroke patients	April 2010	Adults with ischemic or haemorrhagic stroke All interventions were considered irrespective of the number of hours of training and number of hours of constraint/day, duration of treatment, and type of exercise used in training sessions; these data were pooled and discussed under the heading of CIMT	18 RCTs 6 CIMT 10 mCIMT 2 FU	Yes For outcome of disability and arm motor function	Combined studies of CIMT, mCIMT, and FU in meta-analysis of disability and arm motor function Combined results: no effect on disability (0.21 [-0.08, 0.50] I^2=29% n=8 studies Significant effect on arm motor function (0.44 [0.03, 0.84] I^2=64% n=15 studies
Sirtori et al, 2009 (19)	To evaluate the efficacy of CIMT, mCIMT or FU as rehabilitative techniques for upper limb hemiparesis after stroke	June 2008	Adults with ischemic or haemorrhagic stroke	19 RCTs 7 CIMT 11 mCIMT 1 FU	Yes Primary outcome of disability; subgroup analyses on primary outcomes looking at amount of task practice; region of restraint; and time since stroke Secondary outcomes: arm motor function; perceived arm motor function; amount of use; perceived arm motor function; quality of us; arm motor impairment; quality of life	Combined studies of CIMT, mCIMT, and FU in meta-analysis of disability and arm motor function Combined results: significant effect on disability immediately post intervention (0.36 [0.06, 0.65] I^2=not reported n=6 studies Nonsignificant effect on disability at 3 to 6 months follow up (-0.07 [-0.53, 0.40] I^2=not reported, n=2 studies Subgroup analyses: significant effect of task practice ≤ 30 hours (n=4 studies) Significant effect of hand only restraint n=5 studies Non significant effect of time since stroke n=2

Author, Year	Purpose of Review	Search date	Population	Total No. of Studies	Meta-analysis	Conclusion
						studies
French et al, 2008 (18)	To determine effectiveness and cost effectiveness of all forms of repetitive functional task practice	Sept. 2006	Adults who had a stroke	30 RCT 5 CIMT 6 mCIMT 13 RTT 6 TM 1 nRCT 1 RTT	Yes Primary Outcome: Global and limb specific functional measures Secondary Outcome: ADL Adverse outcomes (pain, injury, falls)	Combined interventions (RTT, CIMT, TM) in meta-analysis of disability and arm motor function. Sub group CIMT included mCIMT studies: Significant effect of CIMT (including mCIMT studies) on arm function (0.77 [0.26, 1.29] I^2=41% , n=7 Non significant effect of CIMT (including mCIMT studies) on hand function (0.55, -0.24, 1.34) I^2=0%, n=2

*RCT indicates randomized controlled trial; mCIMT, modified CIMT; RTT, repetitive task training; FU, Forced Use Therapy; TM, treadmill training

Randomized Controlled Trials

Because of the comprehensiveness and current nature of the systematic reviews by Sirtori et al. (14) and Corbetta et al. (17) We selected the RCTs from these reviews that met our inclusion criteria and added any others obtained from our literature search that had been published from 2008 to the present. Thirteen RCTs were therefore included in this evidence-based analysis.

Table 3 reports the characteristics of the 13 RCTs included in this review (3;7;9;10;12;20-27). They include 11 CIMT studies from the systematic review by Sirtori et al. (14), one from the systematic review by Corbetta et al. (17) and one small RCT (3) found during our literature search. Complete details of these studies are reported in Appendix 2. These 13 studies represent the body of evidence for this evidence-based review. All studies were pre and post RCT design with the change scores within the treatment and control groups compared in the final analysis. The sample size ranged from 6 to 60. Seven studies were completed in Asia, 5 in USA, and one in Saudi Arabia. The mean age of participants ranged from 49 to 72 years, and the mean time after stroke when treatment was started ranged from 1 to 32 months. Seven of the 6 studies restrained the arm and hand and 7 studies used a high intensity/short duration program while 6 used a low intensity/long duration program. Regardless of the program, all but one study provided a total of 30 hours of training. The study by Myint et al. (22) provided a total of 40 hours of training. CIMT was delivered by an occupational therapist and/or a physiotherapist in all 14 studies. Usual care included physiotherapy and occupational therapy, with equi-intensity and duration to that of the CIMT group. The follow-up time began immediately after the treatment program ended in all but 2 studies, which include Lin et al, 2010 (3) and Myint et al, 2008. (22)

Table 3: Characteristics of CIMT Studies*

Study	n	Country	Mean Age	Mean Time after Stroke (mos)	Restraint	Training Intensity (hrs/wk)	Training Duration (wks)	Follow-up (wks from start of treatment)
Lin et al, 2010 (3)	13	Taiwan	49	19	Hand	10H	3S	32
Lin et al, 2009 (10)	60	Taiwan	53	21	Hand	10H	3S	3
Myint et al, 2008 (22)	43	China	64	1	Arm and Hand	20H	2S	12
Wu et al, 2007a (9)	30	Taiwan	54	18	Hand	10H	3S	3
Wu et al, 2007b (27)	47	Taiwan	55	12	Hand	10 H	3S	3
Wu et al, 2007c (28)	26	Taiwan	72	8	Hand	10H	3S	3
Lin et al, 2007 (21)	32	Taiwan	58	16	Hand	10H	3S	3
Page et al, 2008 (26)	35	USA	NR	12	Arm and Hand	3H	10L	11
Page et al, 2005 (23)	10	USA	60	1	Arm and Hand	3H	10L	10
Atteya, 2004 (20)	6	Saudi A.	54	5	Arm and Hand	3L	10L	10
Page et al, 2004 (25)	17	USA	59	32	Arm and Hand	3L	10L	10
Page et al, 2002 (24)	14	USA	69	5	Arm and Hand	3L	10L	11
Page et al, 2001 (7)	6	USA	56	5	Arm and Hand	3L	10L	11

*H, High intensity training; L, Low intensity training; S, Short duration; L, Long duration; n, Sample Size

Table 4 reports the outcome measures assessed in each of the 13 studies. Seven studies measured Arm Motor Function with the ARAT scale. Data from 5 studies were available for meta-analysis. Ten studies measured Arm Motor Impairment with the FMA scale; data from 7 studies were available for meta-analysis. All 13 studies measured Perceived Motor Function (both Amount of Use and Quality of Use) using the MAL scale; data from 8 studies were available for meta-analysis. The FIM scale was used to measure activities of daily living (ADL) in 4 studies with all 4 studies having available data for meta-analysis. Finally, 2 studies measured quality of life with the SIS; however, each used a different version of the scale. No study used the Chedoke Arm and Hand Inventory outcome measure.

Table 4: Outcome Measures in Included Studies*

Study	Arm motor function	Arm motor impairment	Perceived motor function	ADL	Quality of life
Lin et al, 2010 (3)		FMA	MAL		
Lin et al, 2009 (10)		FMA Add to forest plot	MAL	FIM	SIS (version 3)
Myint et al, 2008a (22)	ARAT		MAL		
Page et al, 2008 (26)	ARAT	FMA	MAL SD of change not reported.		
Wu et al, 2007a (9)			MAL	FIM	
Wu et al, 2007b (27)		FMA	MAL		
Wu et al, 2007c (28)		FMA	MAL	FIM	SIS (version 2)
Lin et al, 2007 (21)			MAL	FIM	
Page et al, 2005 (23)	ARAT	FMA	MAL		
Atteya, 2004 (20)	ARAT	FMA	MAL SD of change not available		
Page et al, 2004 (25)	ARAT †SD of change not available	FMA SD of change not available	MAL SD of change not available		
Page et al, 2002 (24)	ARAT SD of change not available	FMA SD of change not available	MAL SD of change not available		
Page et al, 2001 (7)	ARAT	FMA	MAL No available data		

*ARAT, action research arm test; MAL, motor activity log; FIM, functional independence measure; FMA, Fugl-Meyer Motor Assessment; SIS, Stroke Impact Scale; SD, standard deviation

Table 5 reports the individual quality assessment of the 13 studies. Sirtori et al. (14) concluded that the studies included in their systematic review had "several methodological weaknesses, did not assess potential harms, had only short-term follow up, were possibly subject to conflicts of interest, and publication bias." Corbetta et al. (17) reported that "the majority of studies were small and likely to be underpowered; the median sample size was 15 patients."

The individual assessments of these 13 studies concluded that sample size ranged from 6 to 60 people in the studies with 8 studies having a sample size of 30 or less. Eight studies had adequate randomization methods and the same number of studies completed a baseline comparison of demographic data which included age, gender, side of brain lesion, and the time-point after onset of stroke to the start of CIMT intervention. While 3 studies reported adequate allocation concealment methodology, it was unclear if this was done in the remaining 10 studies due to lack of reporting. Twelve of the 13 studies reported adequate blinding of the outcome assessor. It was not possible to blind the *treatment* assignment from the study participants, although the study by Lin et al. (21) did report having blinded the study hypotheses from the study participants. It was unclear in all studies whether a sample size calculation was determined a priori. Losses to follow-up were 0 in 9 studies, 10% or less in 2 studies, and unclear in 2 studies. An intention-to-treat analysis was completed in 11 of the 13 studies. These quality parameters have been considered in the study quality criterion of GRADE (see Appendix 3).

Three RCTs did not meet the inclusion criteria for this systematic review. Nevertheless, they are mentioned because they represent study designs which readers may wish to review further. Two studies by Taub et al. (11;29) compared CIMT to a placebo control; the third study by Wolf et al. (30) compared CIMT to usual or customary care (not of equal intensity or duration to that of CIMT) ranging from formal rehabilitation to pharmacologic or physiotherapeutic interventions. In the 2006 study by Taub et al. the placebo control group was designed to control for the duration and intensity of patient-therapist interactions and therapeutic activities. These included a general fitness program with strength, balance, and stamina training, cognitive challenges, and relaxation exercises. However, in the 1993 Taub et al. study, the placebo group—which received two sessions of what was labelled "physical therapy" (comprising a passive range of movement, joint play, muscle tone, and sensory loss) was not of equal intensity and duration to that of CIMT. The study by Wolf et al. which was a multicenter RCT, has been described as a pragmatic study design and thus may have substantial generalizability to real world situations. (Personal communication, Clinical Expert, August 9, 2011) Results of this study indicated that the CIMT group showed a 34% [95% CI, 12%-51%] improvement on the Wolf Motor Function Test (WMFT) compared with the control group, a 0.43 (95% CI, 05-0.8) point increase on the MAL Amount of Use and a 0.48 (95% CI, 0.13-0.84) point increase on the Quality of Movement scale. Similarly, both placebo controlled studies reported significant results in favour of CIMT compared with either placebo group. The quality of these studies will not be evaluated in this report and is left to the reader for review and evaluation.

Table 5: Quality Assessment of RCT Studies

Study	N	Adequate randomization methods	Baseline comparable	Adequate allocation concealment	Blinding of outcome assessors	Sample size calculation	Losses to follow up	Intention to treat analysis
Lin et al, 2010 (3)	13	unclear, no information provided	✓	unclear, no information provided	unclear, no information provided	unclear, no information provided	✓ no losses to follow up	✓
Lin et al, 2009 (10)	60	✓ computerized (block) randomization scheme	✓	✓ opaque numbered envelopes	✓ blinded assessors	unclear, no information provided	✓ no losses to follow up	✓
Myint et al, 2008 (22)	43	✓ "sealed envelopes which were filled at random with indication of which intervention group the patient was allocated to".	✓	✓ "sealed envelopes"	✓	unclear, no information provided	✓ 5/28 in CIMT group; 0/20 in control group	unclear, " modified intention to treat analysis implemented because not all subjects who were randomized received baseline assessment"
Page et al, 2008 (26)	35	✓	✓	unclear	✓	unclear, no information provided	unclear, no information provided about withdrawals	✓
Wu et al, 2007a (9)	13	unclear	✓	unclear	✓	unclear, not reported	✓ no missing data	✓
Wu et al, 2007b (27)	47	✓	✓	unclear	✓	unclear, not reported	✓ no missing data	✓
Wu et al, 2007c (28)	26	✓	✓	unclear	✓	unclear, not reported	✓ no missing data	✓
Lin et al, 2007 (21)	32	✓	✓	✓ sealed envelopes	✓ patients and assessors were blinded to study hypotheses	unclear, no information provided.	✓ 2/17 losses in control group	No, data from 2 patients lost to follow up not included.
Page et al, 2005 (23)	10	✓	reported MAL AOU and MAL QOM, FM and ARA	unclear	✓	unclear, not reported	unclear, no information provided about	yes, results reported for

Study	N	Adequate randomization methods	Baseline comparable	Adequate allocation concealment	Blinding of outcome assessors	Sample size calculation	Losses to follow up	Intention to treat analysis
			scores preintervention was similar with the more affected limb. Statistics not provided				withdrawals	all 10 study subjects.
Atteya, 2004 (20)	6	unclear	reported but not statistically compared	unclear	✓	unclear, not reported	no losses	✓
Page et al, 2004 (25)	17	✓	demographic and clinical baseline data reported but not compared statistically	Unclear	✓	✓	appears no losses as data reported for all study subjects	yes, as data reported for all study subjects
Page et al, 2002 (24)	14	unclear	demographic and clinical baseline data reported but not compared statistically	unclear	✓	unclear, not reported	appears no losses as data reported for all study subjects	✓ yes, as data reported for all study subjects
Page et al, 2001 (7)	6	unclear	subject characteristics reported but not compared statistically	unclear	✓	unclear, not reported	appears no losses as data reported for all study subjects	✓ yes, as data reported for all study subjects

Summary of Existing Evidence

A meta-analysis was completed for the following outcomes:

- Arm motor function measured by the ARAT scale
- Arm motor impairment measured by the FMA scale
- Activities of daily living (ADL) measured by the FIM scale
- Perceived arm motor function measured by the MAL amount of use and quality of use subscales
- Quality of life measured by the stroke impact scale (SIS).

Primary Outcome

Arm Motor Function

Arm motor function was measured using the ARAT scale. Results of 4 studies were combined to derive a pooled-effect estimate and the mean difference was used as a summary statistic. (7;20;23;26) The pooled estimate represents the mean difference in the change scores pre and post treatment in each study group. There is a significant effect of CIMT on arm motor function compared with usual care (Figure 2). All studies used a high intensity/low duration CIMT program, and hand and arm restraint positioning. The mean time after stroke to start of intervention was 1 to12 months. The I^2 value is 38%. Subgroup analysis was not indicated since the I^2 was less than 50% and the individual estimates of effects seemed consistent among studies. The GRADE quality of evidence was assessed as Moderate. Details of the GRADE rating may be found in Appendix 3.

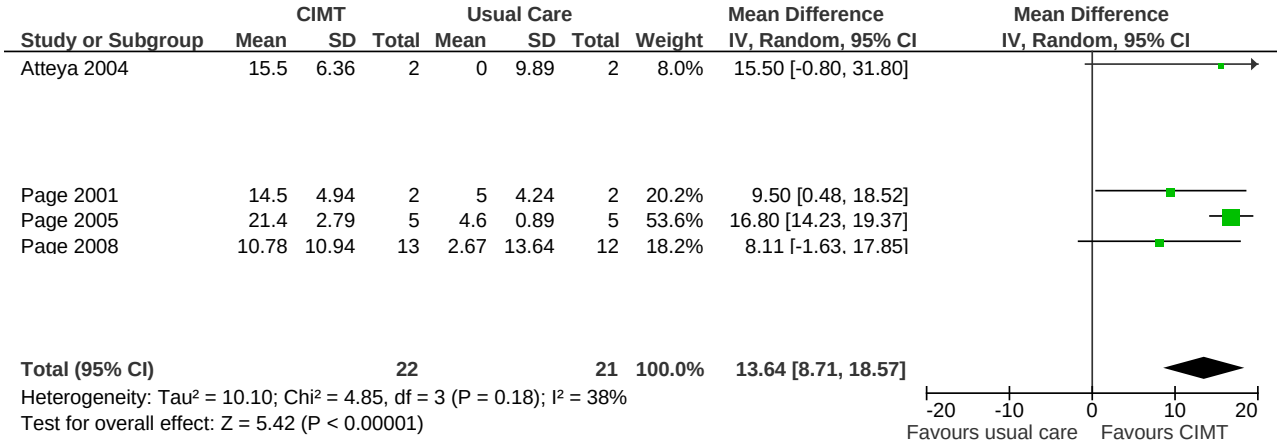

Figure 2: Arm Motor Function Measured using the ARAT

Secondary Outcomes

Arm Motor Impairment

Results of 8 studies were combined to derive a pooled-effect estimate of arm motor impairment and the mean difference was used as the summary statistic. (3;7;10;12;20;23;26;27) All studies measured arm motor impairment with the FMA scale. The pooled estimate represents the mean difference in the change scores pre and post treatment in each group. There is a significant effect of CIMT on arm motor impairment compared with usual care (Figure 3). Heterogeneity is high among the studies as indicated by an I^2 of 83%. Subgroup analyses of these data were completed in order to reduce heterogeneity. The GRADE quality of evidence was assessed as Low. Details of the GRADE rating may be found in

Appendix 3.

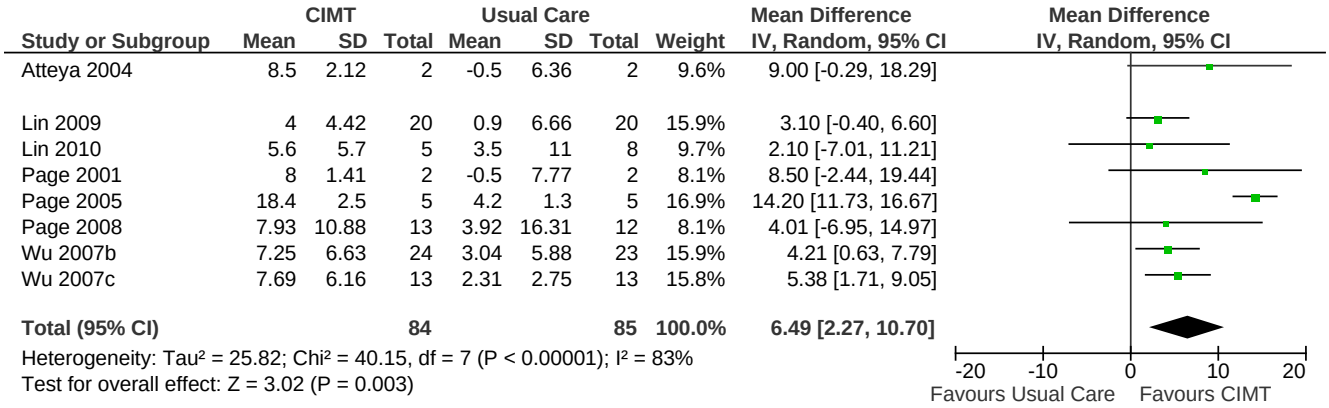

Figure 3: Arm Motor Impairment Measured using the FMA scale

Subgroup Analyses

Table 6 reports the results of the subgroup analyses. A significant effect with acceptable heterogeneity is seen in both the high intensity/short duration program (7;20;23;26) and the low intensity/long duration program. (3;10;12;27) However, the low intensity/long duration program yields the largest effect. Similar results were seen with restraint positioning because the same studies were pooled for the high intensity/short duration program and the hand-only restraint, as well as the low intensity/long duration program and the hand and arm restraint. Heterogeneity was reduced when studies initiating treatment after 12 months from the onset of stroke were pooled. (3;10;27) The forest plots for each of these comparisons are presented in Appendix 4.

Table 6: Arm Motor Impairment Subgroup Analyses*

Subgroup	Program	Restraint Position	Time from Onset of Stroke
High intensity /Short duration Program	RR [95% C.I.] 4.1 [2.1, 6.1] I^2=0% studies=4 n=126		
Low intensity/Long duration Program	RR [95% C.I.] 11.0 [6.3.15.7] I^2=38% studies=4		
Hand		RR [95% C.I.] 4.1 [2.1, 6.1] I^2=0% studies=4 n=126	
Hand and arm		RR [95% C.I.] 11.0 [6.3.15.7] I^2=38% studies=4 n=57	

Subgroup	Program	Restraint Position	Time from Onset of Stroke
1-12 months			RR [95% C.I.] 9.5 [3.6, 15.4] I^2=81% studies=4 n=44
>12 months			RR [95% C.I.] 3.5 [1.1, 6.0] I^2=0% studies=3 n=100

*RR, Relative Risk; C.I., Confidence Interval; n, Sample Size

Activities of Daily Living

Ability to complete activities of daily living was measured using the FIM score in 4 studies. (9;10;12;21) The pooled estimate represents the mean difference in the change scores pre and post treatment in each group. There is a nonstatistically significant effect of CIMT on activities of daily living compared with usual care (Figure 4). Heterogeneity is moderate with an I^2 of 52%. All studies used a high intensity/low duration program and restrained only the hand of the unaffected arm. Three studies (9;10;21) started treatment more than 12 months from the onset of stroke and one study (12) started at less than 12 months. A subgroup analysis was not possible because of the clinical homogeneity among the studies. The GRADE quality of evidence was assessed as Low. Details of the GRADE rating may be found in Appendix 3.

The FIM score is an 18-item scale, grouped into 6 subscales measuring self-care, sphincter control, transfers, locomotion, communication, and social cognition ability. Some items on the scale including sphincter control, communication, and social cognition may not be responsive to CIMT treatment. That is, improvements in these item scores may not be anticipated with CIMT. These items account for up to 50% of the total scale score. (10) Therefore, the lack of statistical significance may be driven by the unresponsive characteristic of some of the scale items.

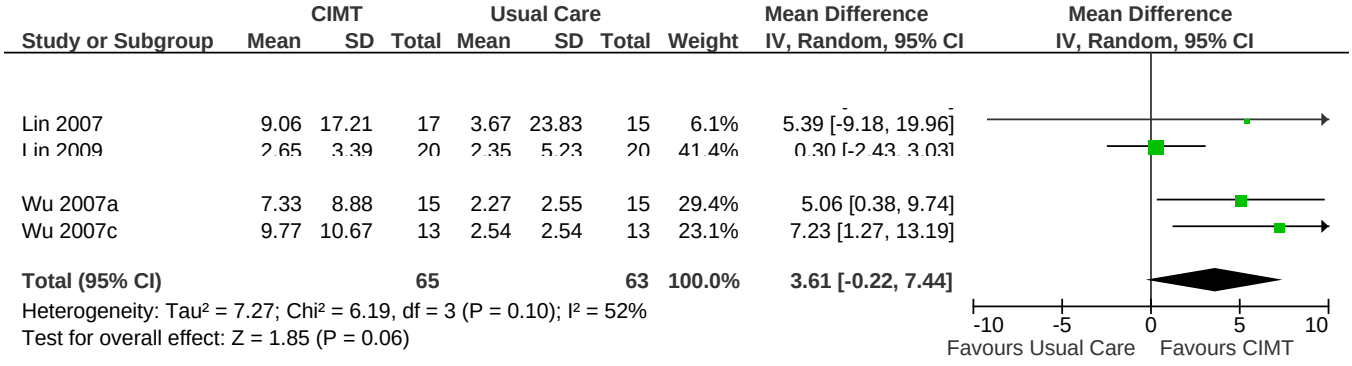

Figure 4: Activities of Daily Living Measured using the FIM scale

Perceived Arm Motor Function (Amount of Use)

Results of 8 studies were combined to derive a pooled-effect estimate of perceived arm motor function in relation to amount of use. (3;9;10;12;21-23;27) All studies measured arm motor function using the MAL Amount of Use scale and therefore the mean difference was used as the summary statistic. The pooled

estimate represents the mean difference in the change scores pre and post treatment in each group. There is a significant effect of CIMT on perceived motor function, and amount of use compared with usual care (Figure 5). Heterogeneity is high among the combined studies as indicated by an I^2 of 91%. Subgroup analyses of these data were completed in order to reduce heterogeneity. The GRADE quality of evidence was assessed as Low. Details of the GRADE rating may be found in Appendix 3.

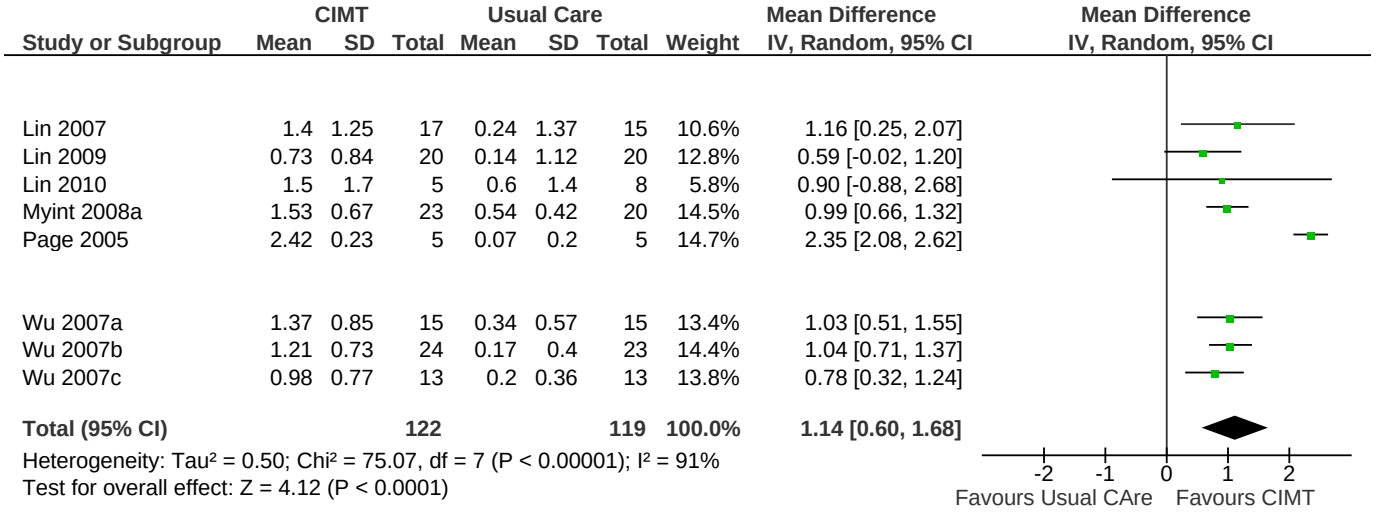

Figure 5: Perceived Arm Motor Function Measured using the MAL Amount of Use Scale

Subgroup Analyses

Table 7 reports the results of the subgroup analyses. A significant effect is seen in both the high intensity/short duration program (3;9;10;12;21;22;27) and the low intensity/long duration program. (23) However, the low intensity/long duration program yields the largest effect, although this is derived from one small study whereas the estimate from the high intensity/short duration program is derived from 7 studies with a pooled sample size of 231 persons. Regarding restraint positioning, heterogeneity is decreased in those studies using hand restraint only. (3;9;10;12;21;27) And similar to arm motor impairment, heterogeneity is reduced if the treatment is started more than 12 months after the onset of stroke. (3;9;10;21) The forest plots for each of these comparisons are presented in Appendix 5.

Table 7: Results of Subgroup Analyses for Perceived Arm Motor Function Amount of Use*

Subgroup	Program	Restraint Position	Time from Onset of Stroke
High intensity /Short duration Program	RR [95% C.I.] 0.95 [0.77, 1.1] I^2=0% studies=7 n=231		
Low intensity/Long duration Program	RR [95% C.I.] 2.4 [2.1, 2.6] I^2=n/a studies=1 n=10		
Hand		RR [95% C.I.] 0.93 [0.72, 1.15] I^2=0% studies=6 n=188	
Hand and arm		RR [95% C.I.] 1.67 [0.34, 3.0] I^2=97% studies=2 n=53	
1-12 months			1.3 [0.52, 2.1] I^2=95% studies=4 n=126
>12 months			0.90 [0.54, 1.25] I^2=0% studies=4 n=115

*RR, Relative Risk, C.I.; Confidence Interval; n, Sample Size

Perceived Arm Motor Function (Quality of Use)

Results of 8 studies were combined to derive a pooled-effect estimate of perceived arm motor function with regard to quality of use. (3;9;10;12;21-23;27) All studies measured perceived arm motor function using the MAL quality of use scale and therefore the mean difference was used as the summary statistic. The pooled estimate represents the mean difference in the change scores pre and post treatment in each group. There is a significant effect of CIMT on perceived motor function quality of use compared with usual care (Figure 6). Heterogeneity is high among the studies as indicated by an I^2 of 61%. Subgroup analyses of these data were completed in order to reduce heterogeneity. The GRADE quality of evidence was assessed as Low. Details of the GRADE rating may be found in Appendix 3.

For this outcome, a sensitivity analysis was completed with the inclusion of the results of the study by Taub et al. (11) This study did not meet the inclusion criteria for the systematic review because it compared CIMT to a placebo group, although the placebo group was of the same intensity and duration as the CIMT group. During the peer review process, therefore, it was suggested that we factor the results of the Taub et al. study into this analysis. (Personal communication, Clinical Expert, August 9, 2011) After doing so, the results indicated a larger statistically significant effect size. (1.10, 95% C.I. 0.73, 1.46)

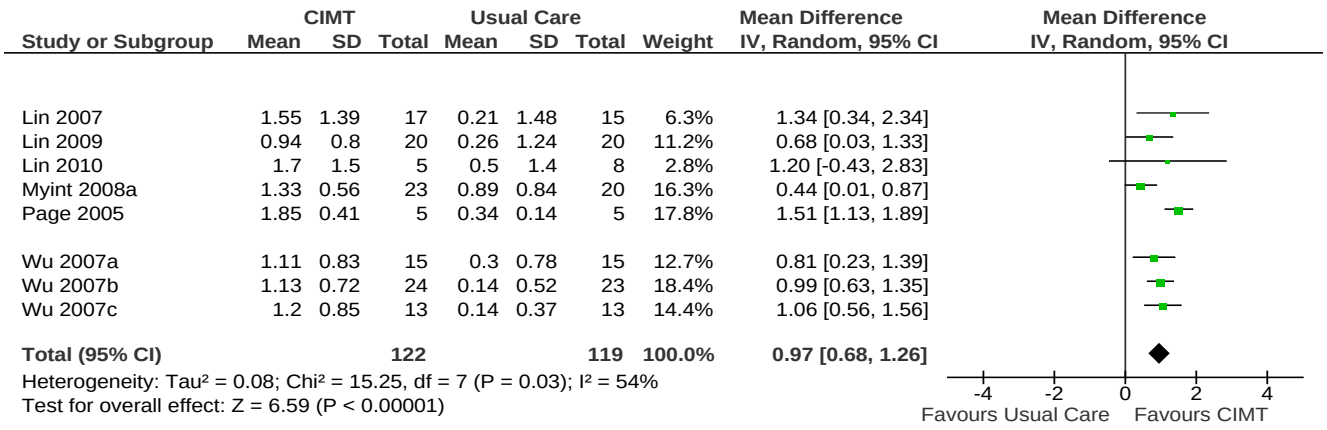

Figure 6: Perceived Arm Motor Function Measured using the MAL Quality of Use Subscale

Subgroup Analyses

Table 8 reports the results of the subgroup analyses. As previously reported for the amount of use scale, a significant effect in quality of use is seen in both the high intensity/short duration program (3;9;10;12;21;22;27) and the low intensity/long duration program. (23) However, while the low intensity/long duration program yields the largest effect, this is derived from one small study, whereas the estimate from the high intensity/short duration program is derived from 7 studies with a pooled sample size of 231 persons. Similar to the amount of use scale, heterogeneity is decreased in those studies using hand restraint only. (3;9;10;12;21;27) And similar to arm motor impairment and perceived arm motor function amount of use subscales, heterogeneity is reduced if the treatment is started more than 12 months after the onset of stroke. (3;9;10;21) The forest plots for each of these comparisons are presented in Appendix 6.

Table 8: Results of Subgroup Analyses for Perceived Arm Motor Function Quality of Use*

Subgroup	Program	Restraint Position	Time from Onset of Stroke
High intensity /Short duration Program	RR [95% C.I.] 0.84 [0.64, 1.1] I^2=1% studies=7 n=231		
Low intensity/Long duration Program	RR [95% C.I.] 1.5 [1.1, 1.9] I^2=n/a studies=1 n=10		
Hand		RR [95% C.I.] 0.96 [0.73, 1.2] I^2=0% studies=6 n=188	

Subgroup	Program	Restraint Position	Time from Onset of Stroke
Hand and arm		RR [95% C.I.] .98[-.07, 2.0] I^2=92% studies=2 n=53	
1-12 months			RR [95% C.I.] 1.0 [0.6, 1.4] I^2=77% studies=4 n=126
>12 months			RR [95% C.I.] 0.86 [0.48, 1.3] I^2=0% studies=4 n=115

*RR, Relative Risk; C.I., Confidence Interval; n, Sample Size

Quality of Life

Two studies measured quality of life but with different versions of the SIS. (10;12) Data were not available to analyze the change scores. Figure 1 reports the mean difference in the final values (post treatment values) in each study for each treatment group. The study by Wu et al. (12) included persons with a mean age of 72 years and a mean time after stroke of 8 months, whereas the study by Lin et al. (10) included persons with a mean age of 53 years who were 21 months poststroke. Both studies were completed in Taiwan. There is a nonstatistically significant difference in quality of life reported in the Wu et al. (12) study and a statistically significant difference reported in the Lin et al. (10) study (Figure 7). The GRADE quality of evidence was assessed as very low. Details of the GRADE rating may be found in Appendix 3.

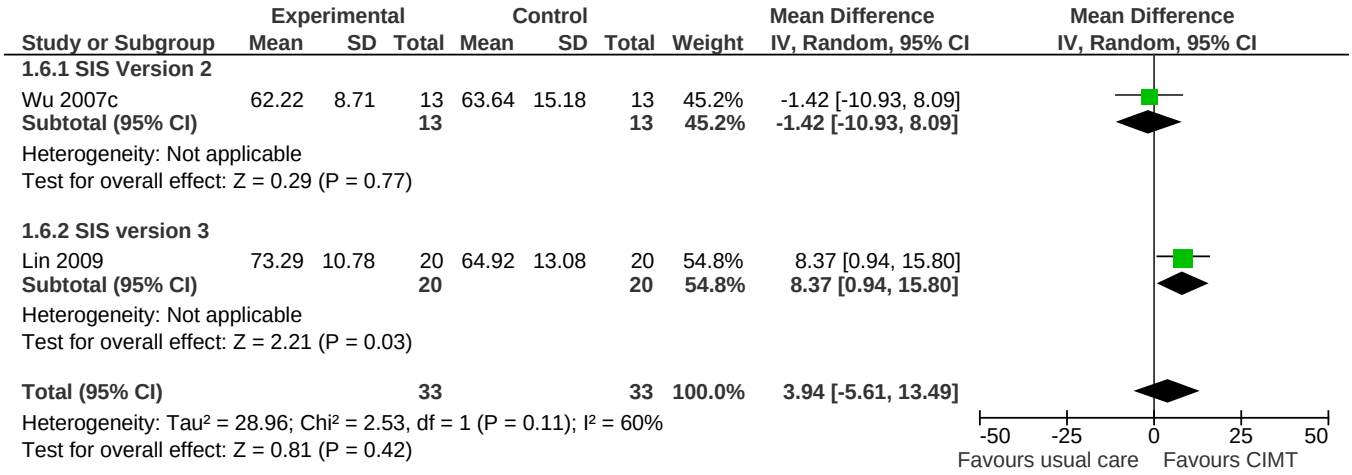

Figure 7: Quality of Life Measured Using the SIS

Summary of Findings

A significant difference with moderate quality evidence was found in our primary outcome of arm motor function in favour of CIMT compared with usual care delivered with the same intensity and duration. Significant differences were also found in 3 of the 5 secondary outcome measures (Table 9). The nonsignificant results may be a factor of a nonresponsive outcome measure (FIM scale) and/or a type II statistical error from an inadequate sample size.

Subgroup analyses identified that starting treatment more than 12 months poststroke may be more effective than starting earlier. However, the effect of the primary outcome was demonstrated in persons starting treatment 1 to 12 months after stroke. Therefore, these data cannot be used to determine whether CIMT is more effective if initiated at a particular time period. A superior effect of a low intensity/long duration program was not demonstrated in subgroup analysis over a high intensity/short duration program. The superiority of one restraining position over another was also not demonstrated.

Table 9: Summary of Meta-analysis Results*

Outcome	Outcome Measure	Number of Studies (n)	Mean Difference in Change Scores CIMT vs. Usual Care [95% C.I.]	Results	Grade Quality of Evidence
Arm Motor Function	ARAT	4 (43)	13.6 [8.7, 18.6]	Significant	Moderate
Arm Motor Impairment	FMA	8 (169)	6.5 [2.3, 10.7]	Significant	Low
Activities of Daily Living	FIM	4 (128)	3.6 [-0.22, 7.4]	Nonsignificant	Low
Self-Reported Amount of Arm Use	Perceived Arm Motor Function Amount of Use Scale	8 (241)	1.1 [0.60, 1.7]	Significant	Low
Self-Reported Quality of Arm Use	Perceived Arm Motor Function (Quality of Use) Scale	8 (241)	0.97 [0.7, 1.3]	Significant	Low
Quality of Life	SIS	2 (66)	3.9 [-5.6, 13.5]	Nonsignificant	Very Low

*C.I., Confidence Interval; n, Sample Size

Existing Guidelines for CIMT

Canadian Best Practice Recommendations for Stroke Care Update 2010

Intensive Constraint-Induced Movement Therapy (CIMT) should not be used for persons in the first month poststroke until further research is completed.

Consider the use of intensive CIMT for a select group of patients who demonstrate at least 20 degrees of wrist extension and 10 degrees of finger extension, with minimal sensory or cognitive deficits. Intensive training should involve restraint of the unaffected arm for at least 90% of waking hours and at least 6 hours a day of intense upper extremity training of the affected arm for 2 weeks.

Consider the use of modified CIMT for a select group of patients who demonstrate at least 20 degrees of wrist extension and 10 degrees of finger extension, with minimal sensory or cognitive deficits. Modified CIMT consists of constraint of the unaffected arm with a padded mitt or arm sling for a minimum of 6 hours a day with 2 hours of therapy for 14 days.

Economic Analysis

Study Question

The objective of this economic analysis is to report costs associated with Constraint-Induced Movement Therapy (CIMT) for rehabilitation of arm dysfunction after stroke in adults in Ontario.

Economic Literature Review

A literature search was performed on February 14, 2011 using OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, OVID EMBASE, Wiley Cochrane, CINAHL, and Centre for Reviews and Dissemination for studies published from 1948 to February week 1, 2011 for MEDLINE; and from 1980 to week 06, 2011 for EMBASE (Appendix 1). Included were studies with full economic evaluations describing both costs and consequences of CIMT and brain or spine injury, or stroke or cerebrovascular accident. The set of search keywords used was the same as that for the clinical systematic review comprising the first part of this evidence-based analysis. According to the clinical systematic review, one health economic evaluation was found comparing the relative cost-effectiveness of CIMT for rehabilitation of arm dysfunction in adult stroke patients.

The study by French et al. (18) in 2008 found that "repetitive functional task practice" which included repetitive task training, treadmill training, and constraint-induced movement therapy, was cost-effective in the United Kingdom at an incremental cost-effectiveness ratio (ICER) of 10,870 GBP per quality-adjusted life year (QALY), provided the net cost per patient was less than 1,963 GBP per QALY. (15) The cost-effectiveness of arm function specifically was calculated as being 15,185 GBP per QALY, which is also considered cost-effective at a willingness-to-pay threshold of 20,000 GBP. The study compared the additional costs of RFTP together with standard care versus standard care alone. However, the study had several limitations. These included the fact that it was based on stroke patient registries from only 2 hospitals in the United Kingdom in 1996 (i.e., limited generalizability); it used the Barthel Index (BI) to estimate overall QALY gains for stroke patients i.e., outcome not specific to arm dysfunction and based on one study linking BI with EQ-5D (a self-reported generic preference-based measure of health, developed by the EuroQol Group in the Netherlands), (28); and it only calculated differences in costs and effects over 3 years (i.e., long-term costs were not considered). Note that in the current analysis, only the incremental costs associated with providing CIMT in addition to "standard" arm dysfunction stroke rehabilitation care in Ontario are examined below.

Ontario-Based Cost Impact Analysis

The 2010 Stroke Evaluation Report by the Institute for Clinical Evaluative Sciences found that approximately 30% of strokes or transient ischemic attacks (TIAs) were treated with stroke rehabilitation care in an inpatient setting, although some experts predicted this proportion should be closer to 40%. (4) The remaining 60%-70% of stroke patients may have received rehabilitation care in an outpatient setting, but the report is unclear about the actual care received by these patients. Note that as a result, the current cost impact analysis was based only on *inpatient* stroke cases and the care received is specifically for arm dysfunction rehabilitation.

The annual number of stroke or TIA inpatients in Ontario in fiscal year (FY) 2011 was estimated from the 2010 ICES Report as being 15,514. This volume of patients was based on stable annual numbers of strokes or TIA inpatients found in Ontario from FY2004 to FY2007. (4) Clinical experts estimated that approximately 40% of stroke inpatients would require rehabilitation for arm dysfunction and about

5%-10% of these patients would be eligible for CIMT programs specifically. As a result, the annual volume of CIMT-eligible stroke patients in Ontario in FY2011 was estimated as being in the range of 349 to 698 patients.

Additional costs of inpatient CIMT stroke rehabilitation for arm dysfunction

The cost of providing CIMT for arm dysfunction in the adult stroke population in Ontario was estimated as an *additional* cost to current stroke rehabilitation care. Through consultation with clinical experts, current care for inpatient stroke rehabilitation for arm dysfunction is approximately 0.5 hours (30 minutes) per patient per day, for 5 days a week. In the current systematic review of effectiveness, a range in intensity (i.e., hours per day, and days per week) was shown to exist for CIMT programs providing arm dysfunction rehabilitation care from 2 hours per day (low intensity) up to 3.5 hours per day (high intensity), to 5 days a week. The length of duration of treatment was also examined and CIMT care was assumed to last for either 2 or 3 weeks (10 or 15 days). For example, the cost of providing "low intensity" CIMT care for arm dysfunction over 3 weeks would consist of 37.5 total hours of stroke rehabilitation care (7.5 hours of current stroke care + 30 hours of CIMT care).

Total estimated costs of inpatient CIMT stroke rehabilitation for arm dysfunction

Given the range in intensity and duration of CIMT, the total cost of providing CIMT in Ontario was calculated for several scenarios listed below. Note that the scenarios are grouped under 2 duration categories representing 10-day and 15-day CIMT programs:

Two-week CIMT program duration (i.e. 10 days over 2 weeks)

a) *Low intensity CIMT programs* provide care to each patient for 2 hours per day, for 10 days over 2 weeks (20 total hours)
b) *Medium intensity CIMT programs* provide care to each patient for 3 hours per day, for 10 days over 2 weeks (30 total hours)
c) *High intensity CIMT programs* provide care to each patient for 3.5 hours per day, for 10 days over 2 weeks (35 total hours)

Three-week CIMT program duration (i.e. 15 days over 3 weeks)

d) *Low intensity CIMT programs* provide care to each patient for 2 hours per day, for 15 days over 3 weeks (30 total hours)
e) *Medium intensity CIMT programs* provide care to each patient for 3 hours per day, for 15 days over 3 weeks (45 total hours)
f) *High intensity CIMT programs* provide care to each patient for 3.5 hours per day, for 15 days over 3 weeks (52.5 total hours)

In order to estimate the total cost of CIMT, the hours shown above are added to the current care hours for inpatient stroke rehabilitation for arm dysfunction. For example, the total hours for each 2-week CIMT program intensity listed above would be *in addition* to the 5 hours of current stroke rehabilitation care already provided to each patient. Likewise, the total hours for each 3-week CIMT program intensity would be added to 7.5 hours of current stroke rehabilitation care.

Costs were estimated by multiplying the total care hours for CIMT by the average hourly wage of an occupational therapist (OT) or physiotherapist (PT). Through expert consultation, it was determined that either an OT or PT could deliver the care required of a CIMT program. According to Statistics Canada's 2006 census, the average annual (total) income of an OT in Ontario was reported as $59,375; the average annual income of a PT in Ontario was reported as $61,962. These annual amounts were divided by the average annual hours worked by OTs and PTs to obtain an average hourly wage: $35.25/hour for OTs ($59,375 / [46.4 weeks per year × 36.3 hours per week]) and $35.50/hour for PTs ($61,962 / [47.3 weeks

per year × 36.9 hours per week]). A final hourly wage estimate of $35.38/hour was used due to the similarity of OT and PT wages as reported in the 2006 census. (31)

Table 10 shows the total costs of combining current rehabilitation care and CIMT for stroke inpatients in Ontario in FY2011. Ranges in costs per patient and total annual costs are shown: approximately $884 per patient for a 2-week (10-day) low intensity CIMT program (annual cost of $0.46 million) to $1,857 per patient for a 3-week (15-day) high intensity CIMT program (annual cost of $0.97 million). Note that these costs represent OT or PT hours spent on stroke rehabilitation for admitted patients. However, CIMT need not occur only in an inpatient setting. According to expert consultation, CIMT would be administered *after* 30 days of inpatient care. In Ontario's current care model, for the first 30 days of inpatient stroke rehabilitation, approximately 10 hours would be spent with patients. Therefore, total costs for CIMT (including current care) may be estimated as follows: for a 2-week (10-day) program with a treatment intensity of 2 hours per day, the total cost would be approximately $0.59 million (349 CIMT-eligible stroke patients); for a 3-week (15-day) program with a treatment intensity of 3.5 hours per day, the total cost would be approximately $1.22 million (698 CIMT-eligible stroke patients).

Table 10: Annual Incremental Costs of CIMT ($ and additional FTEs per year)*

	Per patient cost		Total CIMT-eligible patient costs ($ and FTEs)			
Description	Total care hours	Total cost	FY2011 (low)	FY2011 (high)	Average annual	FTEs
2-week CIMT comparisons (10 days of care)						
Ontario (current care)	5.0	$177	$0.06M	$0.12M	$0.09M	1.5
Low intensity CIMT (2 hrs/day)	25.0	$884	$0.31M	$0.62M	$0.46M	7.6
Medium intensity CIMT (3 hrs/day)	35.0	$1,238	$0.43M	$0.86M	$0.65M	10.7
High intensity CIMT (3.5 hrs/day)	40.0	$1,415	$0.49M	$0.99M	$0.74M	12.2
3-week CIMT comparisons (15 days of care)						
Ontario (current care)	7.5	$265	$0.09M	$0.19M	$0.14M	2.3
Low intensity CIMT (2 hrs/day)	30.0	$1,061	$0.37M	$0.74M	$0.56M	9.2
Medium intensity CIMT (3 hrs/day)	45.0	$1,592	$0.56M	$1.11M	$0.83M	13.7
High intensity CIMT (3.5 hrs/day)	52.5	$1,857	$0.65M	$1.30M	$0.97M	16.0

*Note: "low" and "high" indicates cost estimations based on 349 and 698 CIMT-eligible patients, respectively; FTE represents full-time equivalent figures obtained by dividing the average annual costs by the average annual income of OTs or PTs; FY fiscal year

Appendices

Appendix 1: Literature Search Strategies

Clinical Data Search

Search date: January 21, 2011
Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, OVID EMBASE, CINAHL, Wiley Cochrane, Centre for Reviews and Dissemination/International Agency for Health Technology Assessment

Database: Ovid MEDLINE(R) <1948 to January Week 1 2011>
Search Strategy:

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1 exp Stroke/ or exp Hemiplegia/ (68672)
2 exp Cerebral Palsy/ (12746)
3 exp Dystonia/ (6655)
4 exp Hip Fractures/ (14328)
5 exp Phantom Limb/ (1313)
6 exp Brain Injuries/ (39516)
7 exp Spinal Injuries/ (14488)
8 (spinal injur* or brain injur* or phantom limb or stroke* or cerebrovascular accident* or dystonia or cerebral pals* or (hip adj2 fracture*)).ti,ab. (158867)
9 or/1-8 (238877)
10 exp Restraint, Physical/ or cimt.mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier] (10249)
11 9 and 10 (353)
12 (constraint induced movement therap* or constraint therap*).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier] (236)
13 11 or 12 (445)
14 limit 13 to (english language and humans and yr="2000 -Current") (345)

Database: EMBASE <1980 to 2011 Week 02>
Search Strategy:

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1 exp STROKE PATIENT/ or exp STROKE/ or exp hemiplegia/ (100470)
2 exp cerebral palsy/ (18273)
3 exp focal hand dystonia/ (169)
4 exp hip fracture/ (21253)
5 expagnosia/ (3522)
6 exp brain injury/ (85958)
7 exp spine injury/ (27327)
8 (spinal injur* or brain injur* or phantom limb or stroke* or cerebrovascular accident* or dystonia or cerebral pals* or (hip adj2 fracture*)).ti,ab. (203901)
9 or/1-8 (336778)

10 exp movement therapy/ or cimt.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer] (1691)
11 9 and 10 (491)
12 exp constraint induced therapy/ (220)
13 (constraint induced movement therap* or constraint therap*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer] (348)
14 11 or 12 or 13 (694)
15 limit 14 to (human and english language and yr="2000 -Current") (523)

CINAHL

Top of Form

#	Query	Results
S18	S15 OR S16 Limiters- Published Date from: 20000101-20111231; English Language	276
S17	S15 or S16	310
S16	constraint induced movement therap* or constraint therap*	222
S15	S11 and S14	189
S14	S12 or S13	2668
S13	Cimt	165
S12	(MH "Restraint, Physical")	2507
S11	S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10	66181
S10	(spinal injur* or brain injur* or phantom limb or stroke* or cerebrovascular accident* or dystonia or cerebral pals* or (hip NEAR fracture*))	61071
S9	(MH "Spinal Injuries+")	3074
S8	(MH "Brain Injuries+")	10361
S7	(MH "Phantom Pain")	209
S6	(MH "Phantom Limb")	196
S5	(MH "Hip Fractures")	2890
S4	(MH "Focal Hand Dystonia")	177
S3	(MH "Cerebral Palsy")	4296
S2	(MH "Hemiplegia")	2355
S1	(MH "Stroke") OR (MH "Stroke Patients")	22887

Economics Data Search

Search date: February 14, 2011
Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, OVID EMBASE, CINAHL, Wiley Cochrane, Centre for Reviews and Dissemination/International Agency for Health Technology Assessment

Database: Ovid MEDLINE(R) <1948 to February week 1 2011>
Search Strategy:

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1 exp Stroke/ or exp Hemiplegia/ (69176)
2 exp Cerebral Palsy/ (12817)
3 exp Dystonia/ (6676)
4 exp Hip Fractures/ (14399)
5 exp Phantom Limb/ (1320)
6 exp Brain Injuries/ (39685)
7 exp Spinal Injuries/ (14580)
8 (spinal injur* or brain injur* or phantom limb or stroke* or cerebrovascular accident* or dystonia or cerebral pals* or (hip adj2 fracture*)).ti,ab. (159918)
9 or/1-8 (240214)
10 exp Restraint, Physical/ or cimt.mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier] (10299)
11 9 and 10 (356)
12 (constraint induced movement therap* or constraint therap*).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier] (239)
13 11 or 12 (448)
14 limit 13 to (english language and humans and yr="2000 -Current") (348)
15 exp Economics/ (426503)
16 exp Models, Economic/ (7555)
17 exp Resource Allocation/ (13390)
18 exp "Value of Life"/ or exp "Quality of Life"/ (90377)
19 (econom$ or cost$ or budget$ or pharmacoeconomic$ or pharmaco-economic$ or valu$).ti. (190156)
20 ec.fs. (275839)
21 ((cost$ adj benefit$) or costbenefit$ or (cost adj effective$) or costeffective$ or econometric$ or life value or quality-adjusted life year$ or quality adjusted life year$ or quality-adjusted life expectanc$ or quality adjusted life expectanc$ or sensitivity analys$ or "value of life" or "willingness to pay").ti,ab. (65657)
22 or/15-21 (731258)
23 13 and 22 (24)
24 limit 23 to (english language and yr="2000 -Current") (19)

Database: EMBASE <1980 to 2011 Week 06>
Search Strategy:

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1 exp STROKE PATIENT/ or exp STROKE/ or exp hemiplegia/ (104145)
2 exp cerebral palsy/ (18498)
3 exp focal hand dystonia/ (175)
4 exp hip fracture/ (21437)
5 expagnosia/ (3545)
6 exp brain injury/ (86524)
7 exp spine injury/ (27511)
8 (spinal injur* or brain injur* or phantom limb or stroke* or cerebrovascular accident* or dystonia or cerebral pals* or (hip adj2 fracture*)).ti,ab. (207811)
9 or/1-8 (341967)
10 exp movement therapy/ or cimt.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer] (1734)
11 9 and 10 (512)
12 exp constraint induced therapy/ (226)
13 (constraint induced movement therap* or constraint therap*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer] (365)
14 11 or 12 or 13 (721)
15 limit 14 to (human and english language and yr="2000 -Current") (529)
16 exp "Health Care Cost"/ (157193)
17 exp Health Economics/ (487916)
18 exp Resource Management/ (22761)
19 exp Economic Aspect/ or exp Economics/ or exp Quality Adjusted Life Year/ or exp Socioeconomics/ or exp Statistical Model/ or exp "Quality of Life"/ (1079733)
20 (econom$ or cost$ or budget$ or pharmacoeconomic$ or pharmaco-economic$ or valu$).ti. (223220)
21 ((cost$ adj benefit$) or costbenefit$ or (cost adj effective$) or costeffective$ or econometric$ or life value or quality-adjusted life year$ or quality adjusted life year$ or quality-adjusted life expectanc$ or quality adjusted life expectanc$ or sensitivity analys$ or "value of life" or "willingness to pay").ti,ab. (86283)
22 or/16-21 (1231577)
23 14 and 22 (80)
24 limit 23 to (english language and yr="2000 -Current") (77)

CINAHL

#	Query	Results
S20	S18 and S19	116
S19	(MH "Economics+") or (MH "Resource Allocation+") or MW ec or (MH "Quality of Life+") or (econom* or cost* or budget* or pharmacoeconomic* or pharmaco-economic* or valu*) or ((cost* N1 benefit*) or costbenefit* or (cost N1 effective*) or costeffective* or econometric* or life value or quality-adjusted life year* or quality adjusted life year* or quality-adjusted life expectanc* or quality adjusted life expectanc* or sensitivity analys* or "value of life" or "willingness to pay")	510393
S18	S15 OR S16 Limiters - Published Date from: 20000101-20111231; English Language	279

S17	S15 or S16	313
S16	constraint induced movement therap* or constraint therap*	224
S15	S11 and S14	192
S14	S12 or S13	2691
S13	Cimt	169
S12	(MH "Restraint, Physical")	2526
S11	S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10	66922
S10	(spinal injur* or brain injur* or phantom limb or stroke* or cerebrovascular accident* or dystonia or cerebral pals* or (hip NEAR fracture*))	61734
S9	(MH "Spinal Injuries+")	3113
S8	(MH "Brain Injuries+")	10515
S7	(MH "Phantom Pain")	213
S6	(MH "Phantom Limb")	203
S5	(MH "Hip Fractures")	2928
S4	(MH "Focal Hand Dystonia")	177
S3	(MH "Cerebral Palsy")	4354
S2	(MH "Hemiplegia")	2386
S1	(MH "Stroke") OR (MH "Stroke Patients")	23218

Appendix 2: Characteristics of Included Studies

Table A1: Characteristics of Included Studies

Study	Time Point	Dosage of Task Practice (hrs)	CIMT Treatment Components	Control Components	Outcome Measures
Lin et al, 2010 (3) N=13 Taiwan	At least 3 months after a stroke Average time 18.3 months	30	Restraining mitten for 6 hours/day Training for 2 hours/day for 5 days/week for 3 weeks Shaping Dosage of Task Practice: #wks x # session/wk x session duration= 3 x 5 x 2 = 30 hours	Traditional rehabilitation matched to the dCIT in duration and intensity. 2 hour therapy sessions were patients were engaged in neurodevelopmental treatments including balance training, stretch of the affected limb, weight bearing with the affected limb, and fine-motor tasks in addition to practice of activities of daily living with the unaffected side.	Perceived arm motor function: MAL Motor impairment recovery: UL subscale of the FMA
Lin et al, 2009 (10) N=60 Taiwan	6 months poststroke	30	Restraining mitten for 6 hours/day Training for 2 hours/day of functional task practice for 5 sessions/week for 3 weeks. Performed at home practice. Shaping: level of task was adapted based on patient ability and improvement during training. #wks x # session/wk x session duration= 3 x 5 x 2 = 30 hours	Bilateral arm training worked the simultaneous movements of both the affected and unaffected UL in functional tasks in symmetric or alternating patterns for 2 hours/weekday for 3 weeks. These functional tasks also emphasized UL movements involved in ADL and focused on both UL moving synchronously. The group did not perform at home practice Control group controlled for duration and intensity of patient therapist interactions and therapeutic activities (2 hours/day, 5 days/week for	ADL measure: FIM Arm motor impairment: FMA Perceived arm motor function: MAL Quality of life: SIS

Study	Time Point	Dosage of Task Practice (hrs)	CIMT Treatment Components	Control Components	Outcome Measures
				3 weeks). Therapy involved training for hand function, coordination, balance, and movements of the affected UL, as well as compensatory practice on functional tasks with the unaffected UL and both ULs.	
Myint et al, 2008 (22) China n=43	2-16 weeks poststroke	40	Restraining sling for 90% of waking hours Training for 4 hours/day 5 days/week for 10 days Shaping #wks x # session/wk x session duration= 2 x 5 x 4 =40 hours	4 hours of conventional OT and PT using a combination of neurodevelopmental techniques in the geriatric day hospital. Bimanual tasks for upper limbs, compensatory techniques for ADL, strength and range of motion, positioning and mobility training.	Motor function: functional test for hemiparetic upper extremity, ARAT Perceived arm motor function: MAL Dexterity: Nine-hole peg test ADL measures: modified Barthel Index
Page et al, 2008 (26) n=35 USA	More than 1 year ago	30	Restraining arm every weekday for 5 hours with a cotton sling and hands placed in mesh mitten Training: 30 minutes each of PT and OT 3 times/week for 10 weeks. PT used upper limb stretching, dynamic stand/balance activities and gait training. Shaping #wks x # session/wk x session duration= 10 x 3 x 1 = 30 hours	Traditional Rehab group: 30 minutes of consecutive PT and OT sessions, 3 days/week for 10 weeks. Approximately 80% of each PT and OT session focused on proprioceptive neuromuscular facilitation techniques emphasising functional tasks where possible, stretching of the affected limb. 20% was focused on compensatory techniques using the less affected side Control group received no therapy during the 10 week period.	Arm motor function: ARAT Perceived arm motor function: MAL Arm motor impairment: FMA

Study	Time Point	Dosage of Task Practice (hrs)	CIMT Treatment Components	Control Components	Outcome Measures
Wu et al, 2007c (28) n=26 Taiwan	0.5-31 months poststroke	30	Restraint of hand and wrist with mitt for 6 hours. Training: 2 hours/day, 5 times/week for 3 weeks. Functional tasks chosen by the patient and the treating therapist including turning on and off the light switch, reaching forward to move a jar from one place to another, picking up a cup and drinking from it, a hairbrush and combing hair and other ADL activities. Shaping and adaptive and repetitive task practice techniques were used during training sessions #wks x # session/wk x session duration= 3 x 5 x 2 = 30 hours	Traditional Rehab received therapy for equal time and intensity to the CIMT group. 2 hours/day, 75% focused time on neurodevelopmental techniques emphasizing functional task practice as well as stretching of the affected limb, weight bearing with the affected limb and fine motor dexterity activities. 25% focused on compensatory techniques of the unaffected limb to perform functional tasks and assist the affected limb during the task performance.	Perceived arm motor function: MAL Arm motor impairment: FMA ADL measure: FIM Quality of life: SIS
Wu et al, 2007b (27) n=47 Taiwan	3-37 months poststroke	30	Restraint by a mitt for 6 hours/day throughout study period. Training: 2 hours/day, 5 days/week for 3 consecutive weeks) All participants received routine interdisciplinary stroke rehabilitation separate from the study treatment during regularly scheduled OT sessions. 1.5 hours/day for 5days/week. Shaping assumed same protocol as Wu, 2007a. #wks x # session/wk x session duration= 3 x 5 x 2 = 30 hours	Traditional therapy involved neurodevelopmental therapy emphasizing functional task practice when possible, stretching and weight bearing with the more affected arm and fine motor dexterity training.	Arm motor impairment: FMA Perceived arm motor function: MAL Kinematic variables

Study	Time Point	Dosage of Task Practice (hrs)	CIMT Treatment Components	Control Components	Outcome Measures
Wu et al, 2007a (9) n=30 Taiwan	12-36 months poststroke	30	Restraining mitten for 6 hours/day Training for 2 hours/day, 5 days/week for 3 weeks Shaping #wks x # session/wk x session duration= 3 x 5 x 2 = 30 hours	The Traditional Rehab group received training matched to the CIMT group in duration and intensity of OT activities. Routine rehab continued as well. The group received 2 hour therapy sessions, engaged in neurodevelopmental treatments emphasizing balance training, stretching of the affected limb, and fine-motor tasks in addition to practice on ADL with the less affected side.	Perceived arm motor function: MAL Kinematic variables
Lin et al, 2007 (9) n=32 Taiwan	16 months (mean) after stroke	30	Restraining mitten for 6 hours/day Training of the affected arm for 5 days/week for 2 hours/day for 3 consecutive weeks Shaping: level of challenge was adapted based on patient ability and improvement during the training #wks x # session/wk x session duration= 3 x 5 x 2= 30 hours	Traditional rehabilitation with same duration and intensity as CIMT group (5 days/week for 2 hours/day for 3 consecutive weeks). Therapy included strength, balance, and fine motor dexterity training, functional task practice, and stretching/weight bearing by the affected arm.	Perceived arm motor function: MAL Global function measure: FIM Kinematic variables
Page et al, 2005 (23) n=10 USA	Ischemic stroke less than 14 days	30	Restraining arm every weekday for 5 hours with a cotton sling and hands placed in mesh mitten Training: 30 minutes of PT and OT each 3 times/week for 10 weeks. PT used upper limb stretching, dynamic stand/balance activities and gait training. Shaping #wks x # session/wk x session	Traditional Rehab: 3days/week for 10 weeks, patients received standard therapy in the inpatient unit of the hospital for 30 minutes. Therapy included stretching of affected limb, weight bearing with affected limb, manual dexterity exercises and ADLs with the less affected side.	Arm motor function: ARAT Perceived arm motor function: MAL Arm motor impairment: FMA

Study	Time Point	Dosage of Task Practice (hrs)	CIMT Treatment Components	Control Components	Outcome Measures
			duration= 10 x 3 x 1 = 30 hours		
Atteya, 2004 (20) n=4 Saudi	4-6 months poststroke	30	Restraining arm using a cotton Bobath sling. Training: half hour of each of OT and PT 3 times/week for 10 weeks Shaping #wks x # session/wk x session duration= 10 x 3 x 1 = 30 hours	Traditional therapy received half hour each of OT and PT	ADL: FUGL Arm Motor function: ARA Motor Function: WMFT Perceived arm motor function: MAL
Page et al, 2004 (25) n=17 USA	More than 1 year	30	Restraining arm every weekday for 5 hours with a cotton sling and hands placed in mesh mitten Training: 30 minutes of PT and OT each 3 times/week for 10 weeks. PT used upper limb stretching, dynamic stand/balance activities and gait training. Shaping #wks x # session/wk x session duration= 10 x 3 x 1 = 30 hours	Traditional Rehab group: 30 minutes of consecutive PT and OT sessions, 3 days/week for 10 weeks. Approximately 80% of each PT and OT session focused on proprioceptive neuromuscular facilitation techniques emphasising functional tasks where possible, stretching of the affected limb. 20% was focused on compensatory techniques using the less affected side Control group received no therapy during the 10 week period.	Arm motor function: ARAT Perceived arm motor function: MAL Arm motor impairment: FMA
Page et al, 2002 (24) n=14 USA	4 weeks to 6 months poststroke	30	Restraining every weekday for 5 hours with a cotton sling for arm and hands placed in mesh mitten. Training: 30 minutes of PT and OT	Regular therapy group received 30 minutes of OT and PT sessions 3 times /week for 10 weeks. Given	Motor function: ARAT Perceived arm motor function: MAL Arm motor impairment: FMA

Study	Time Point	Dosage of Task Practice (hrs)	CIMT Treatment Components	Control Components	Outcome Measures
			each 3 times/week for 10 weeks. OT used functional tasks for the affected upper limb. PT used upper limb stretching, dynamic stand/balance activities and gait training. Shaping #wks x # session/wk x session duration= 10 x 3 x 1 = 30 hours	neuromuscular facilitation principles during the PT and OT sessions, some compensatory techniques were taught. No therapy group did not receive any interventions, therapy programs, or exercise programs for 10 weeks.	
Page et al, 2001 (7) n=6 USA	4 weeks to 6 months poststroke	30	Restraining with a cotton Bobath sling of lower arm and hands every weekday for 5 hours Training: 30 minutes of OT and PT each 3 times/week for 10 weeks 80% of the time was dedicated to neuromuscular facilitation techniques with emphasis on ADL tasks and 20% on compensatory techniques using the unaffected side Shaping #wks x # session/wk x session duration= 10 x 3 x 1 = 30 hours	Usual care group received 30 minutes of OT and PT each 3 times/week for 10 weeks. 80% of the time was dedicated to neuromuscular facilitation techniques with emphasis on ADL tasks and 20% on compensatory techniques using the unaffected side No therapy group during the same 10-week period	Arm motor function: ARAT, WMFT2 Perceived arm motor function: MAL ARM motor impairment: FMA

Appendix 3: GRADE Profile

Table A1: GRADE Profile

Quality assessment							Summary of findings		
							No. of patients		
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	CIMT	Usual Care	Quality
Arm Motor Function (Better indicated by higher values)									
4	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	strong association[3]	22	21	⊕⊕⊕◯ MODERATE
Arm Motor Impairment (Better indicated by higher values)									
8	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	serious[5]	none	84	85	⊕◯◯◯ LOW
FIM Score (Better indicated by higher values)									
4	randomized trials	serious[6]	no serious inconsistency	very serious[7]	no serious imprecision	Confounding did not reduce effect[8]	65	63	⊕◯◯◯ LOW
Perceived Motor Function (AOU) (Better indicated by higher values)									
8	randomized trials	very serious[9]	no serious inconsistency	no serious indirectness	no serious imprecision	none	122	119	⊕◯◯◯ LOW
Perceived Motor Use (QOU) (Better indicated by higher values)									
8	randomized trials	very serious[9]	no serious inconsistency	no serious indirectness	no serious imprecision	none	122	119	⊕◯◯◯ LOW
Quality of Life (Better indicated by higher values)									
2	randomized trials	serious[10]	serious[11]	no serious indirectness	serious[12]	none	33	33	⊕◯◯◯ VERY LOW

[1] Allocation concealment is unclear, Atteya, 2004 (20), Page, 2005 (23), 2001 (7), Page, 2008 (26). Unclear randomization in Page, 2001 (7), and Atteya, 2004 (20).
[2] Wide confidence intervals, small sample sizes.
[3] No explanation was provided.
[4] Unclear randomization methods, Page, 2001 (7), Atteya, 2004 (20) Lin 2010 (3); unclear allocation concealment, Atteya,2004 (20), Lin, 2010 (3), Page, 2001 (7), 2005 (23), 2008 (26), Wu, 2007b (27), and 2007c. (28)
[5] Heterogeneity, I-squared is 81%, 5 of the 8 studies have estimates consistent with important harms and important benefits.
[6] Allocation concealment unclear, Wu, 2007a (9) and 2007c (28); adequate randomization unclear Wu, 2007a (9)
[7] Some items on the FIM score may not respond to CIMT including sphincter control, communication, social cognition. These items make up almost 50% of total score.
[8] 50% of FIM score may be unresponsive to effects of CIMT, however, there is a strong trend in favour of CIMT with this outcome despite this confounding.
[9] Unclear allocation concealment in 2 studies including Lin, 2010 (3), Wu, 2007a (9); unclear randomization methods in Lin, 2010 (3), Wu, 2007a (9), 2007b (27), 2007 c (28); self-reported measure which may be a bias since the patient could not be blinded to treatment group.
[10] Self- reported measure, patients were not blinded to treatment.
[11] Inconsistency in statistical effect between studies.
[12] Both studies have a small sample size.

Appendix 4: Arm Motor Impairment Subgroup Analyses

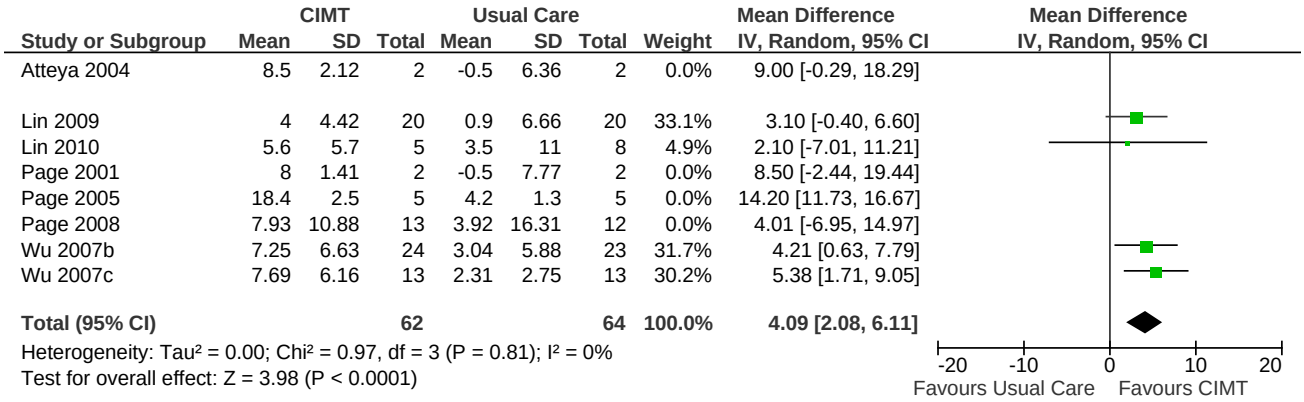

Figure 1: Arm Motor Impairment in Studies Using a High Intensity/Short Duration Program

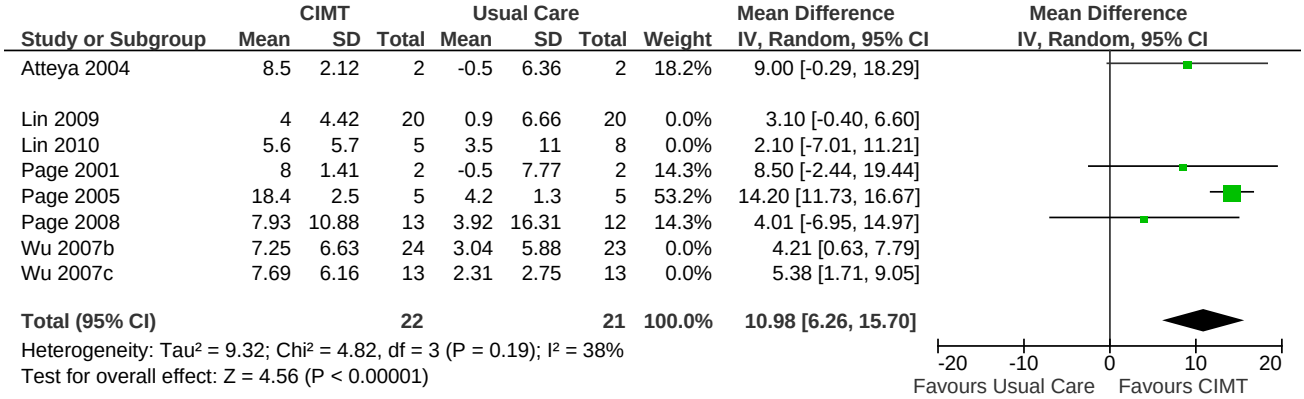

Figure 2: Arm Motor Impairment in Studies Using a Low Intensity/Long Duration Program

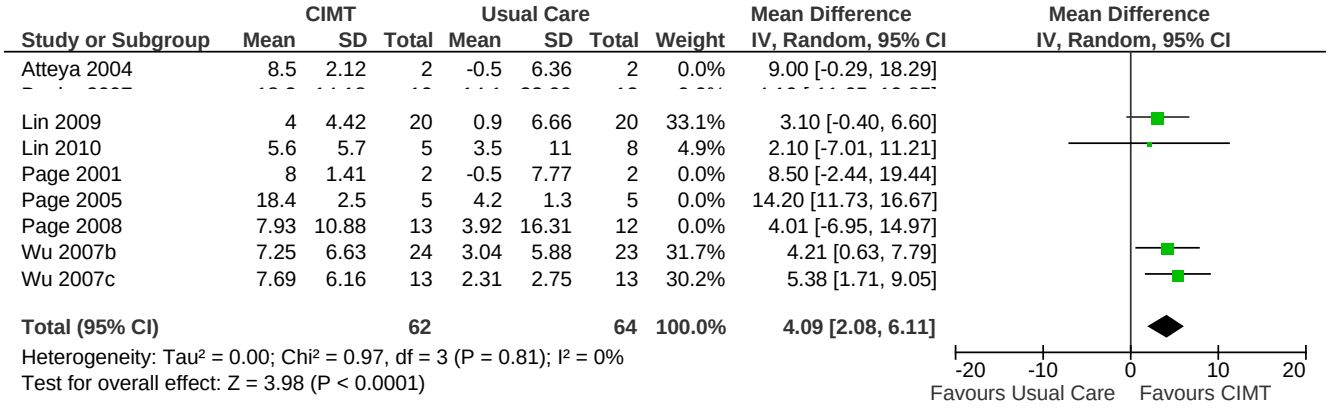

Figure 3: Arm Motor Impairment in Studies Using Hand Restraint Only

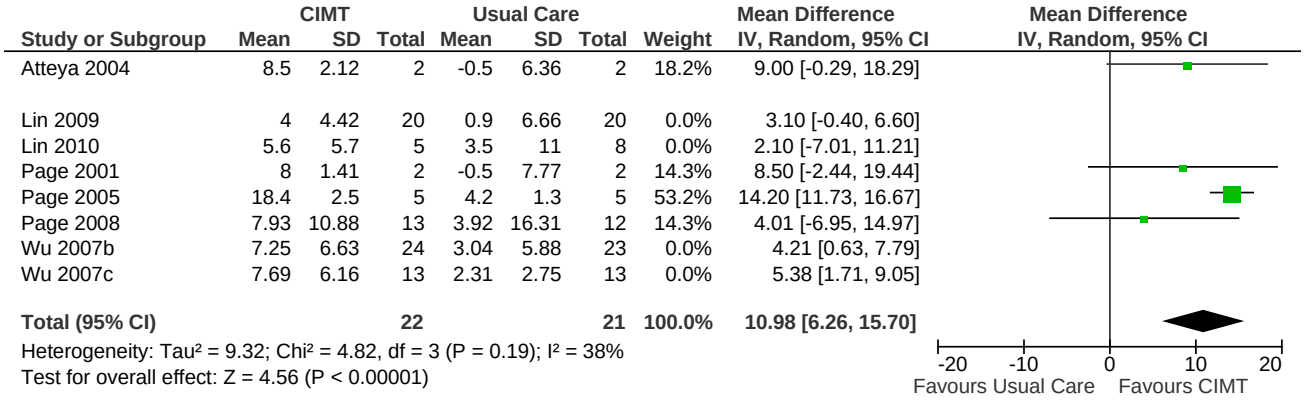

Figure 4: Arm Motor Impairment in Studies Using Hand and Arm Restraint

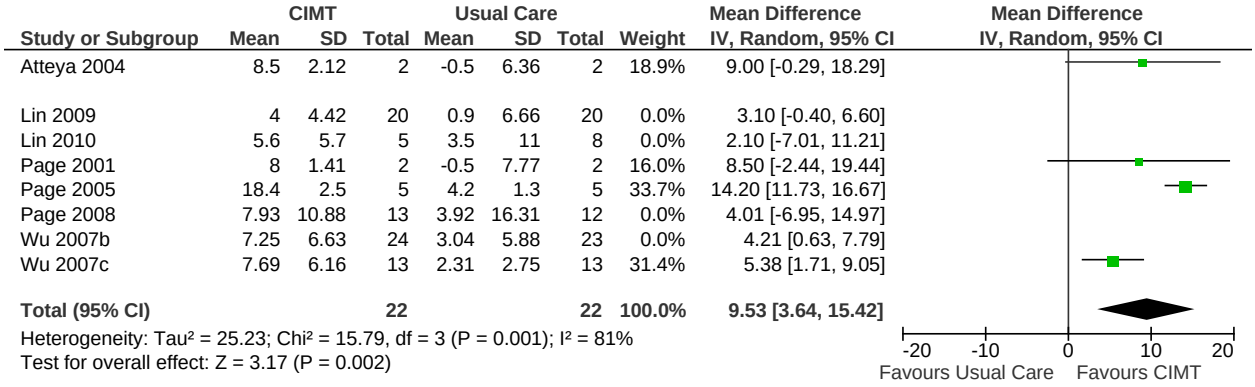

Figure 5: Arm Motor Impairment in Studies Starting Treatment 1-12 Months (mean) After Onset of Stroke

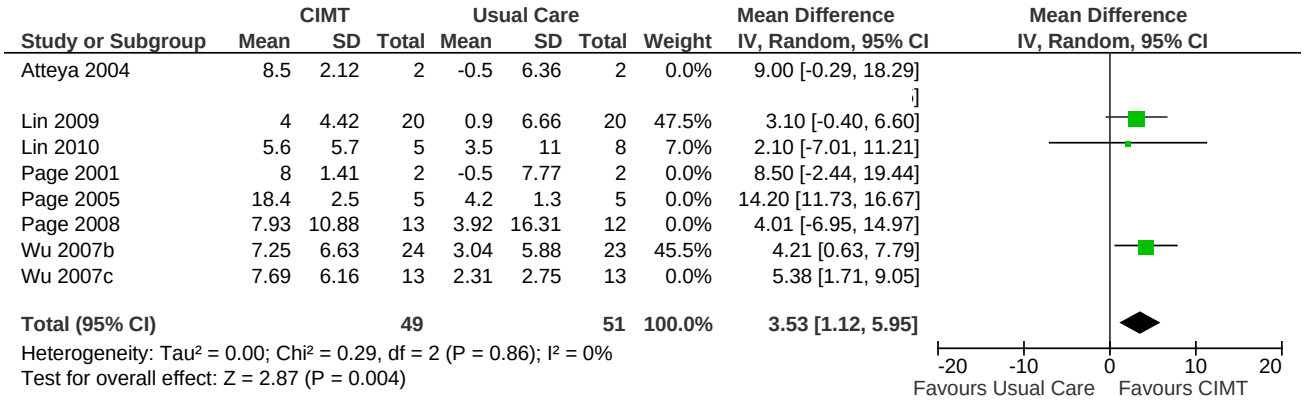

Figure 6: Arm Motor Impairment in Studies Starting Treatment > 12 Months (mean) After Onset of Stroke

Appendix 5: Perceived Arm Motor Function Amount of Use Subgroup Analyses

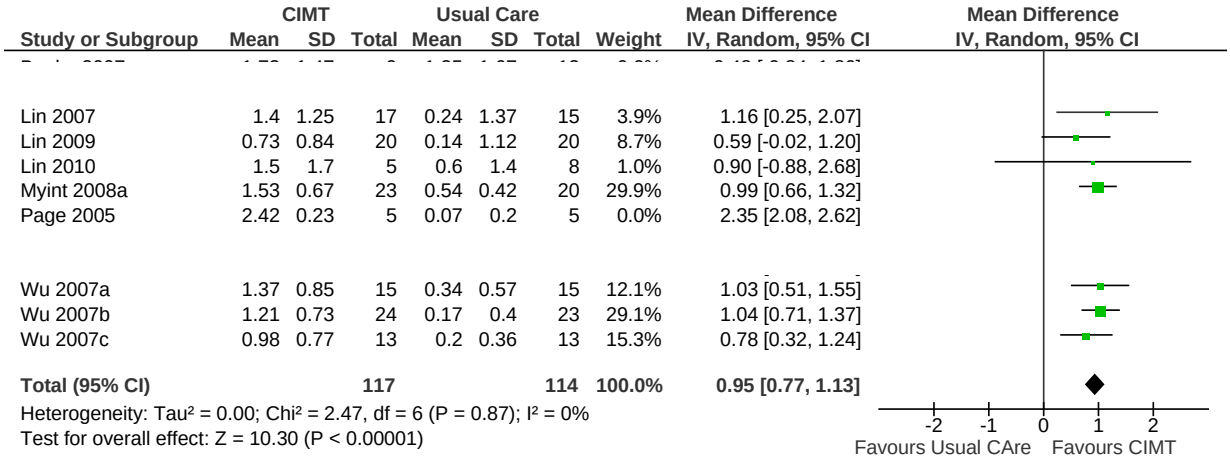

Figure 7: Perceived Arm Motor Function in Studies Using a High Intensity/Short Duration Program

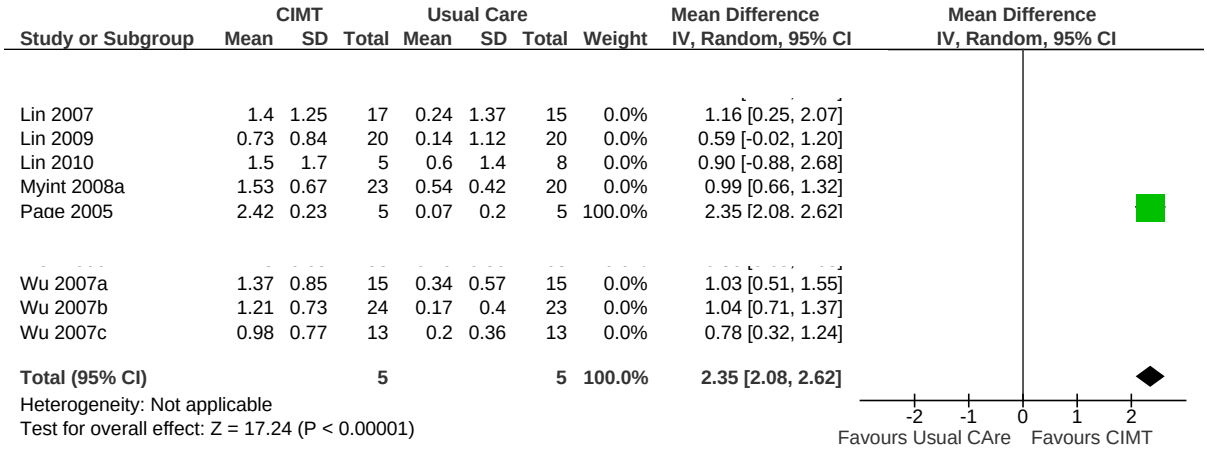

Figure 8: Perceived Arm Motor Function in Studies Using a Low Intensity/Long Duration Program

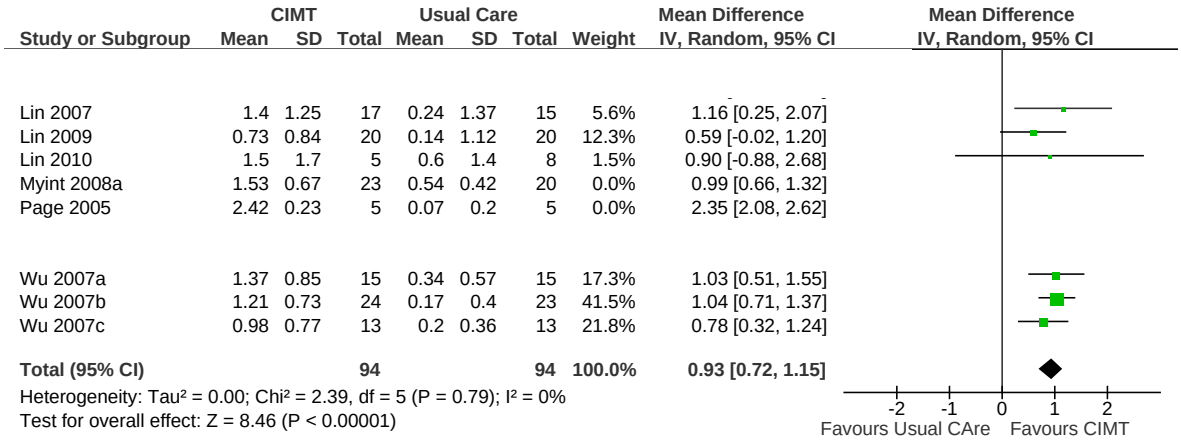

Figure 9: Perceived Arm Motor Function in Studies Using Hand Restraint Only

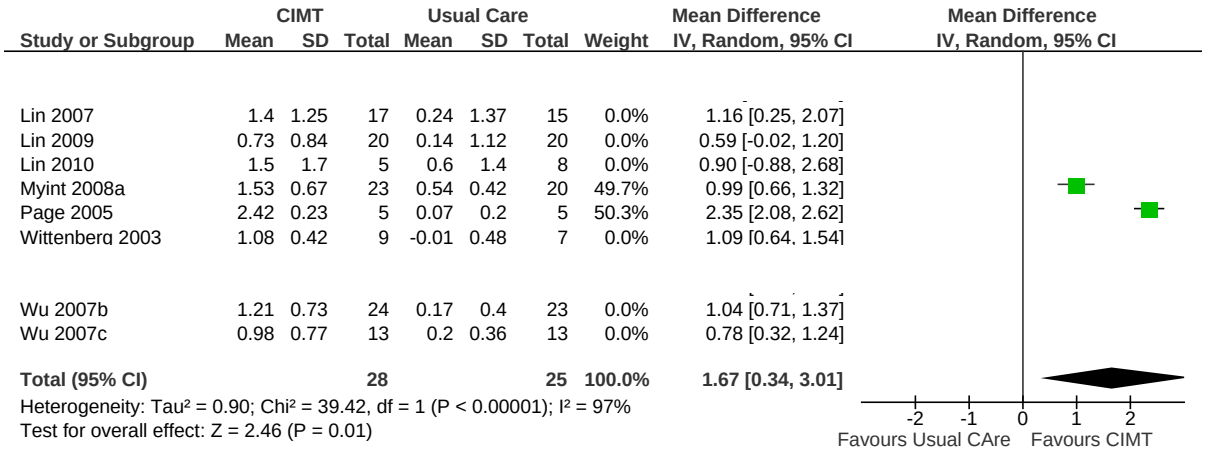

Figure 10: Perceived Arm Motor Function in Studies Using Arm and Hand Restraint

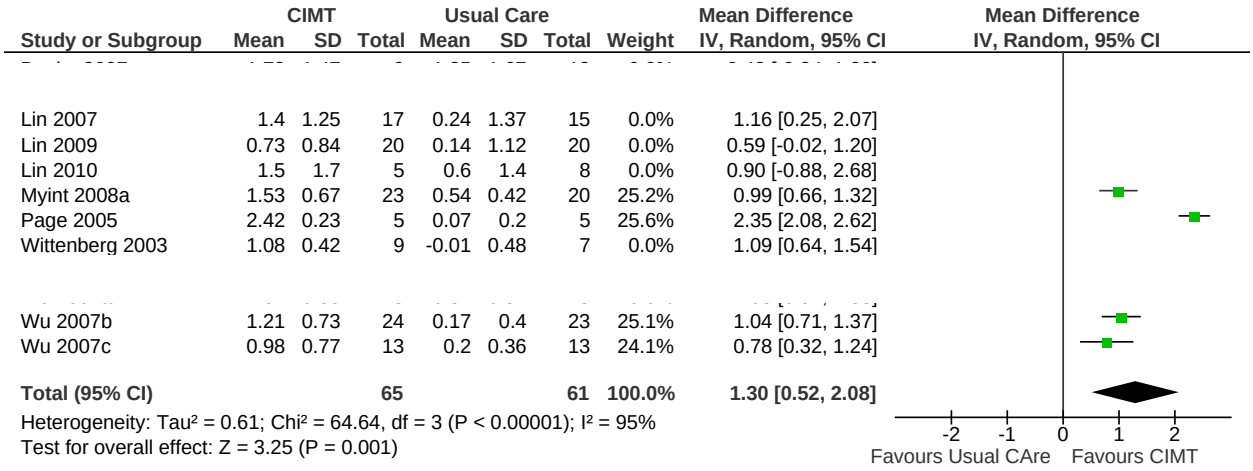

Figure 11: Perceived Arm Motor Function in Studies Starting Treatment 1-12 Months After Onset of Stroke

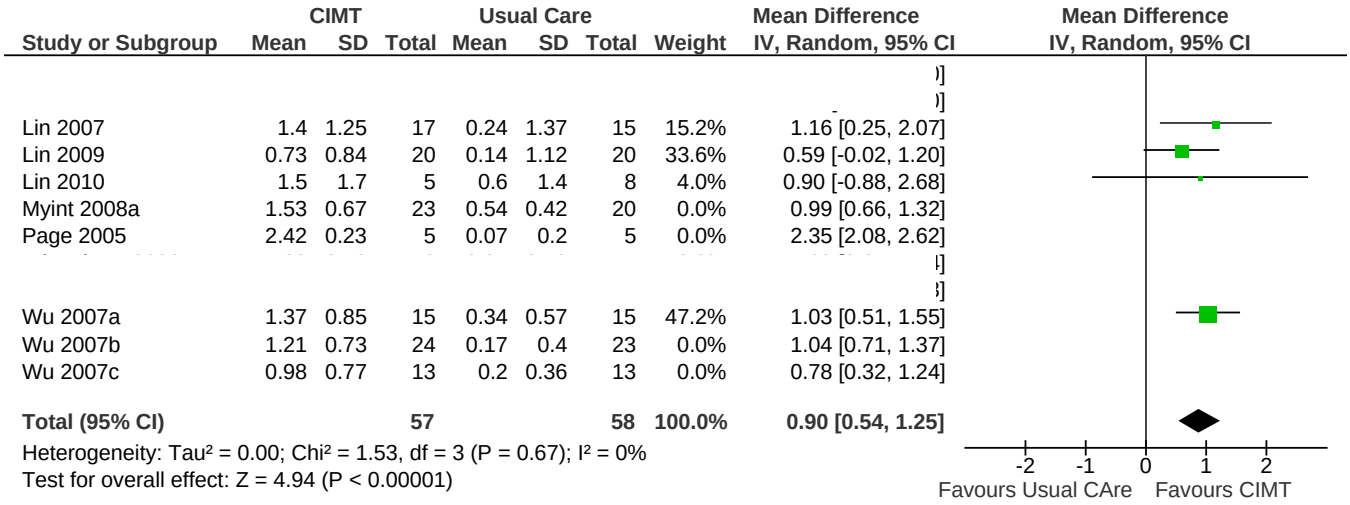

Figure 12: Perceived Arm Motor Function in Studies Starting Treatment >12 Months After Onset of Stroke

Appendix 6: Perceived Arm Motor Function Quality of Use Subgroup Analyses

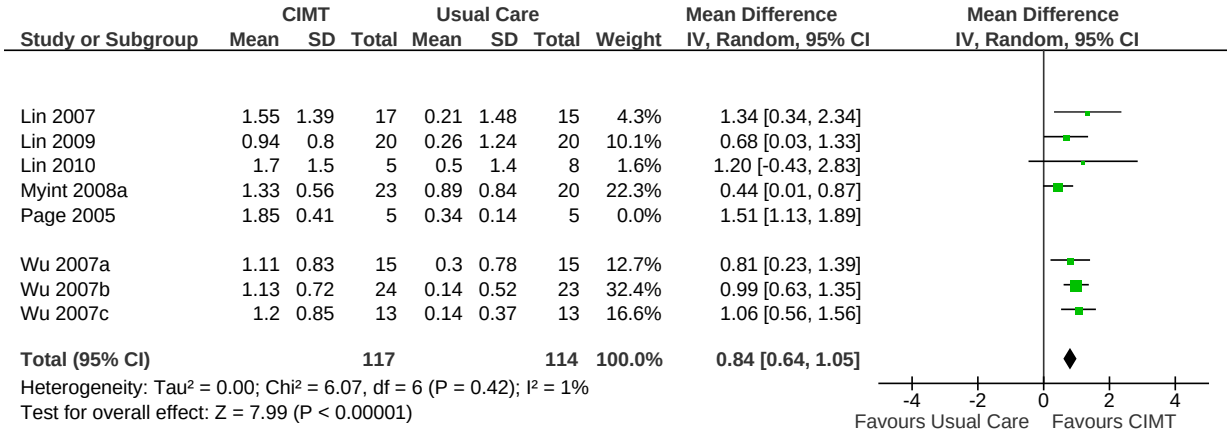

Figure 1: Perceived Arm Motor Function in Studies Using a High Intensity/Short Duration Program

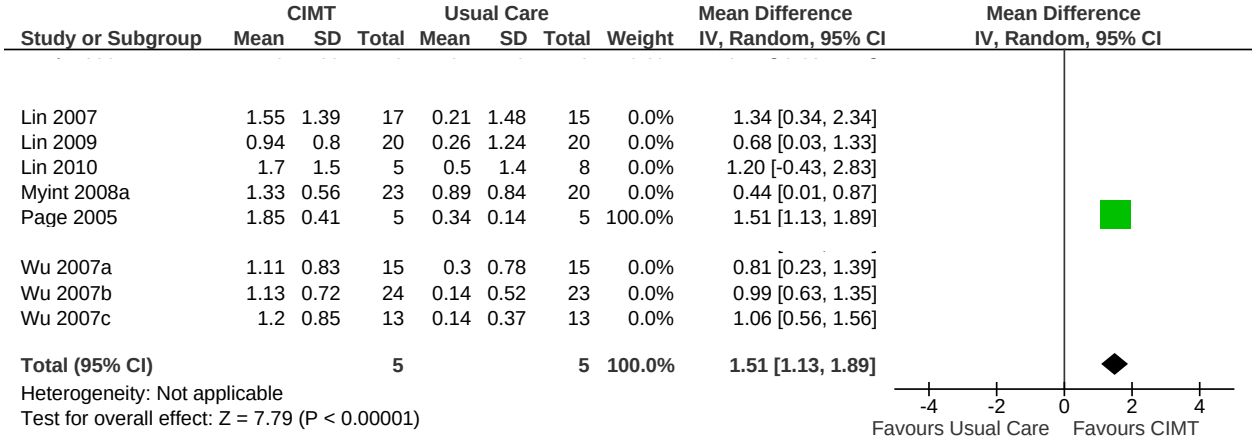

Figure 2: Perceived Arm Motor Function in Studies Using a Low Intensity/Long Duration Program

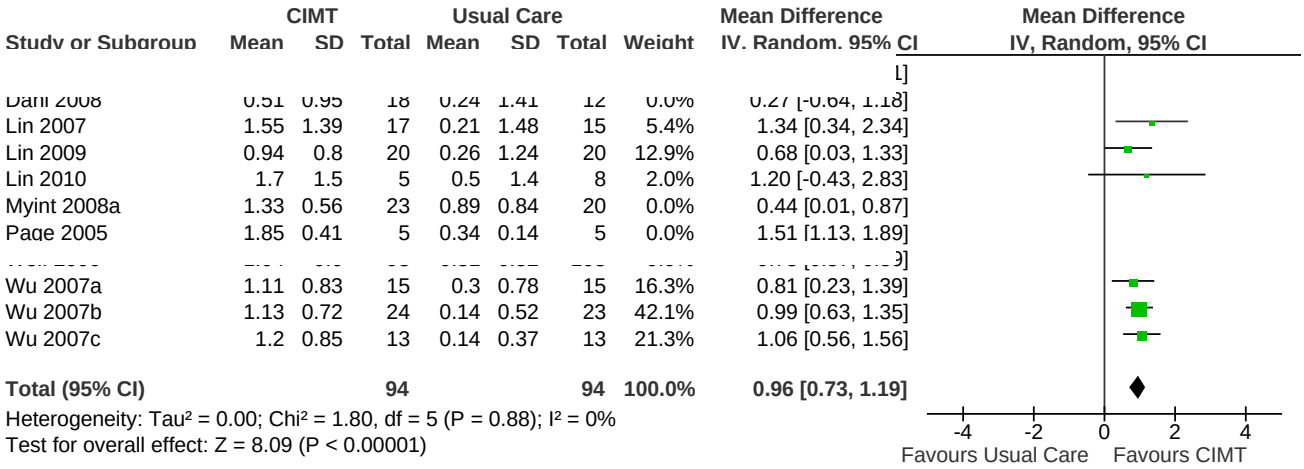

Figure 3: Perceived Arm Motor Function in Studies Using Hand Restraint Only

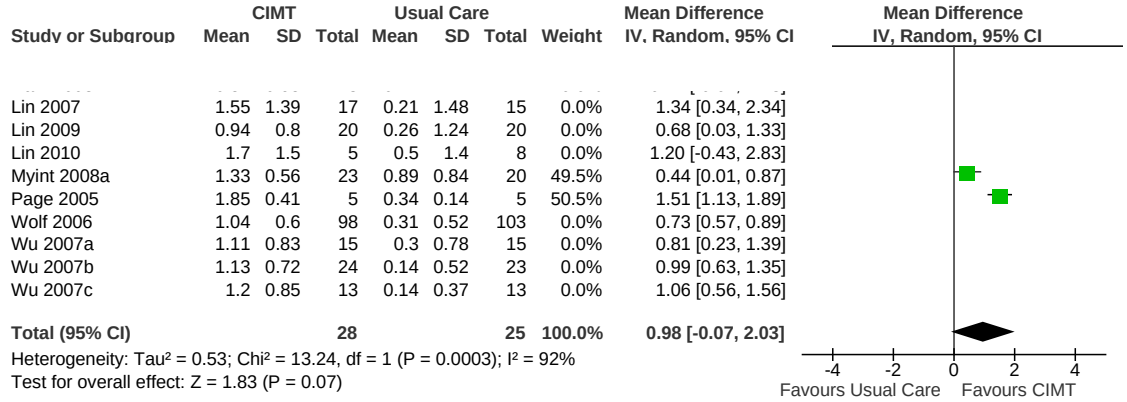

Figure 4: Perceived Arm Motor Function in Studies Using Arm and Hand Restraint

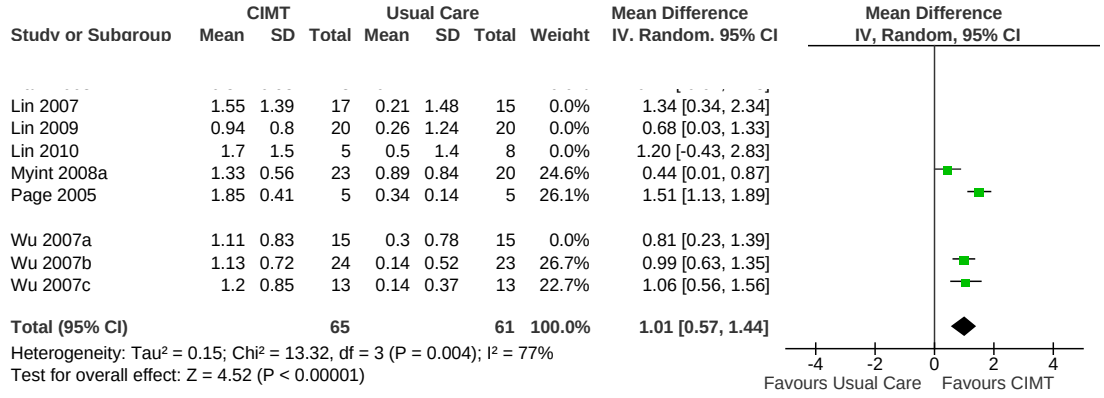

Figure 5: Perceived Arm Motor Function in Studies Starting Treatment 1-12 Months After Onset of Stroke

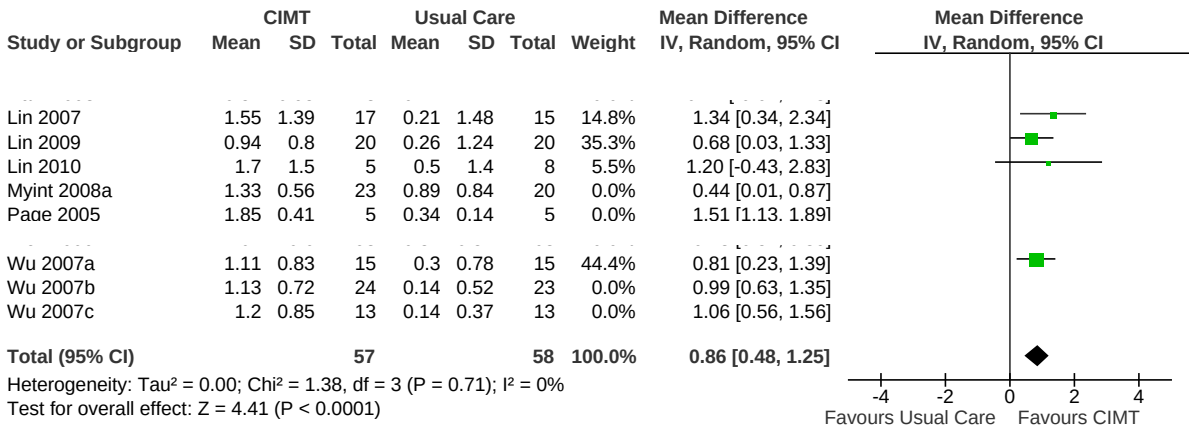

Figure 6: Perceived Arm Motor Function in Studies Starting Treatment >12 Months After Onset of Stroke

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