Stroke is the number one cause of long-term disability in the United States\(^1\) and 30-66% of stroke patients show motor deficits in the arm contralateral to the lesion after six months.\(^2\) Lack of upper extremity control, specifically arm and hand movement, can directly affect quality of life.\(^2\) Compensatory strategies and motor relearning have been used to progress plasticity-based motor performance following a stroke, specifically practice and repetition type exercises.\(^4\) Passive movement is insufficient to alter motor recovery, so active engagement attempts that focus on coordination, rather than strengthening, have been proven most effective.\(^1\)

Rehabilitation is key to minimizing disability after stroke; use of the affected body part for task-related challenges is critical for cortical neural reorganization in long-term rehabilitation for individuals with chronic stroke.\(^1\) With the aid of a physiotherapist, rehabilitation can be effective in minimizing disability post-stroke, particularly on the hemiplegic (affected) side. Neurorehabilitation techniques, such as task-oriented bilateral arm training (BAT), allow individuals to practise activities with the upper limbs in a simultaneous manner. The basic premise of BAT is that symmetrical bilateral movements activate similar neural networks in both hemispheres as homologous muscle groups are simultaneously activated.\(^1\) Consequently, bilateral symmetrical movements allow the activation of the undamaged hemisphere to increase activation of the damaged hemisphere to facilitate movement control of the impaired limb.\(^1\) Therefore, BAT should promote neural plasticity.\(^1\) Compared to BAT, unilateral movements (e.g., unilateral arm training, UAT) generate an interhemispheric inhibition in the ipsilateral hemisphere that prevents mirror movements in the opposite contralateral hemisphere.\(^1\)

Evidence supporting the effectiveness of BAT, as compared to other therapies such as UAT, is conflicting.\(^1\) While many of the reports have been generally negative, some report conflicting or
inconsistent results, which may be attributed to a number of confounding variables including level of impairment, therapy intensity, and phase of stroke recovery. Historically, neurorehabilitation was thought to plateau in the chronic phase of stroke (≥6 months post stroke); however, Teasell et al. report that functional gains can be made when therapies are provided during this time. There exists an abundance of literature which provides evidence for interventions long after the typical recovery phase which supports the notion that motor improvement beyond the acute/sub-acute phase may be possible. Thus, the objective of the current study was to conduct a systematic review and meta-analysis of all randomized controlled trials (RCTs) examining BAT on motor function among individuals with chronic stroke (≥6 months).

Methods

Literature Search Strategy

Relevant articles were identified by a literature search of articles published from January 2000 to December 2013 using multiple databases (i.e., MEDLINE, CINAHL, EMBASE, PsycINFO, Cochrane Central Register of Controlled Trials, OT Seeker). Key words used included stroke, cerebral vascular accident, hemorrhage, ischemic, bilateral arm training, bilateral upper limb training, upper limb, upper extremity, chronic and stroke bilateral/bimanual coordination/training, motor recovery/rehabilitation, motor control/coordination, and interlimb coordination. References of retrieved articles were also searched to identify additional articles that may have been missed in the primary database search.

Study Selection

Two authors (RM, AM) independently assessed titles, abstracts, and full length articles against inclusion criteria. Studies were included for analysis if the following six a priori criteria were met:

1) published in English;
2) included only human subjects;
3) research design was a RCT;
4) treatment group received bilateral arm treatment and the control group received a form of rehabilitation therapy representing ‘typical’ or ‘usual’ rehabilitation for the upper limb;
5) mean time since stroke was ≥6 months for both the treatment and control groups; and
6) functional improvement of the upper-extremity was assessed pre-treatment and post-treatment using a measurable outcome.

Studies were excluded from analysis if BAT was provided alongside another treatment (e.g., electrical stimulation) or if the control group provided a treatment not ‘typically’ used in a rehabilitation setting. Furthermore, studies were eliminated if data could not accurately be extracted from the article or if a complete explanation of the BAT protocol was not available.

Study Appraisal

Each RCT was assessed for methodological quality using the Physiotherapy Evidence Database (PEDro) scoring system. Scores were extracted from the PEDro website (www.pedro.org.au) where possible. Scores that were not available online were independently calculated by two authors (RM, CK). The PEDro scale consists of 11 questions that are answered with either a “yes” (1 point) or “no” (0 points). Since the first question is not included in the final score, a maximum score of 10 can be achieved. Strength of evidence was assessed using previously established guidelines for the Evidence-Based Review of Stroke Rehabilitation, (where “excellent” quality RCTs are scored as 9 or 10 on the PEDro, “good” quality studies as 6–8, “fair” quality studies as 4 or 5; and “poor” quality studies as 1-3). The PEDro was originally developed to assess physiotherapy trials however, the tool has subsequently been used to evaluate rehabilitation trials in the stroke population. Additionally, it has demonstrated both good reliability and validity.22

Data Synthesis

Extracted data included subject demographics (e.g., age, gender, time since injury), sample size, treatment and control methods, outcome measures, and study results. If data could be extracted, it was summarized in a table. Where necessary and when possible, authors of selected studies were contacted to collect additional raw data. If accurate data could not be extracted from the study or collected from the original author(s), it was not included in the meta-analysis on that particular outcome measure. Meta-analyses for individual outcome measures were conducted using the software Comprehensive Meta-Analysis Version 2 (Biostat Inc., Englewood, New Jersey, USA, 2007). Baseline (pre-treatment) and follow-up (post-treatment) scores in mean ± standard deviation form were extracted for both the treatment and control groups. In the event that a standard deviation was not available, standard errors were converted to standard deviations, or a p value or Cohen’s d value was used. In the instance that there were two control groups, only the data from the control group receiving ‘usual’ care was included in the meta-analysis. To quantify the effect of heterogeneity, an F² value was calculated which provides a measure
of the degree of inconsistency in study results. $I^2$ is readily calculated from basic results obtained from a typical meta-analysis as $I^2 = \frac{100\% \times (Q - df)}{Q}$, where Q is Cochran’s heterogeneity statistic and df the degrees of freedom. A value of 0% indicates no observed heterogeneity, and larger values show increasing heterogeneity. A pooled mean difference (MD) ± standard error (SE: 95% confidence interval, CI) was calculated between the treatment and control groups. To enhance clinical relevance, effect sizes were converted into their original units. Statistical significance was set at p<0.05.

Five meta-analyses were conducted on the following outcome measures: Fugl-Meyer Assessment (FMA); Functional Independence Measure (FIM); Motor Active Log Amount of Use (MAL AOU); Motor Active Log Quality of Movement (MAL QOM); and the Modified Motor Assessment Scale (MAS). For each outcome measure assessed, the baseline (pre-treatment) and follow-up (post-treatment) mean ± standard deviation was extracted for both the treatment and control groups.

Each of the five outcome measures analysed in the meta-analyses were specific to evaluating functional motor ability of the upper limb. The FMA evaluates and measures recovery in post-stroke hemiplegic patients and is a uniform system of measurement for disability based on the International Classification of Impairment, Disabilities and Handicap. The FIM is similar to the FMA, and more specifically measures the level of patient disability and indicates the level of assistance that is required for the individual to carry out activities of daily living. The MAL is used to assess how stroke survivors use their more-impaired arm outside the laboratory. Finally, the MAS is used to assess everyday motor function in stroke patients.

Results

Study Quality and Characteristics

Eight studies met inclusion criteria (Figure 1). Table 1 displays study characteristics, interventions, outcome measures and results for the included studies. The RCTs were published from 2004 to 2011 and PEDro scores ranged from 1 to 7. Samples sizes ranged from 8 to 92 with a total pooled sample size of 274 subjects. On average, subjects were 48.31 months post stroke and had a mean age of 57.63 years. All patients were randomized to either a treatment group (BAT) or a control group. The control therapies included dose-matched UAT

Movement therapy or physical therapy (PT). The following outcome measures were most commonly reported by the included studies and were analyzed in the meta-analyses: FMA, FIM, MAL AOU, MAL QOM, and MAS. No adverse events were reported by any of the studies.

Heterogeneity

The FMA used a fixed effects model due to the low $I^2$ value and the relatively small number of studies used to calculate the effect size (Q-value=6.625; df(Q)=4.000; $I^2=39.619$). The FIM (Q-value=0.038; df(Q)=2.000; $I^2=0.000$), MAL AOU (Q-value=0.163; df(Q)=2.000; $I^2=0.000$), MAL QOM (Q-value=0.105; df(Q)=2.000; $I^2=0.000$) and MAS (Q-value=0.005; df(Q)=1.000; $I^2=0.000$) analyses demonstrated complete homogeneity; therefore, a fixed effects model was used.

Analysis 1: FMA

Five studies that used FMA to score upper limb impairment were included in a meta-analysis (Figure 2). The FMA showed significant improvement in motor impairment whereby the BAT groups improved, on average, 3.77 points whereas the control group improved just 1.23 points (MD=1.46; SE=0.662; p=0.028).
### Bilateral Arm Training in Stroke

<table>
<thead>
<tr>
<th>Study</th>
<th>PEDro-Evidence</th>
<th>Country</th>
<th>Sample Size</th>
<th>Protocol</th>
<th>Control Group</th>
<th>Treatment Group</th>
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<tbody>
<tr>
<td>Lin et al.</td>
<td>6-Good</td>
<td>Taiwan</td>
<td>20</td>
<td>3h/5d. wk for 6 wk</td>
<td>FMA</td>
<td>BAT (n=10)</td>
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<tr>
<td>Lin et al.</td>
<td>7-Excellent</td>
<td>Taiwan</td>
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<td>BAT (n=20)</td>
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<td>Liu et al.</td>
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<td>USA</td>
<td>10</td>
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<td>FMA</td>
<td>BAT (n=10)</td>
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<tr>
<td>Whittall et al.</td>
<td>6-Good</td>
<td>USA</td>
<td>10</td>
<td>3h/5d. wk for 6 wk</td>
<td>FMA</td>
<td>BAT (n=10)</td>
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<tr>
<td>Wu et al.</td>
<td>6-Good</td>
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<td>3h/5d. wk for 6 wk</td>
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<tr>
<td>Ross et al.</td>
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<td>3h/5d. wk for 6 wk</td>
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<td>BAT (n=10)</td>
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<tr>
<td>Summerville et al.</td>
<td>6-Good</td>
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<td>3h/5d. wk for 6 wk</td>
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<td>BAT (n=10)</td>
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<td>Summerville et al.</td>
<td>7-Excellent</td>
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<td>3h/5d. wk for 6 wk</td>
<td>FMA</td>
<td>BAT (n=10)</td>
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</table>

### Outcome Tool

- FMA
- AOU/QOM

### Summary of Results

<table>
<thead>
<tr>
<th>Study</th>
<th>Age XSD</th>
<th>Stroke Onset XSD</th>
<th>Outcome Tool</th>
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<tbody>
<tr>
<td>Lin et al.</td>
<td>53.5±13.2</td>
<td>13±6.8</td>
<td>FMA</td>
</tr>
<tr>
<td>Lin et al.</td>
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<td>25±20.3</td>
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<tr>
<td>Liu et al.</td>
<td>63±15.3</td>
<td>75±(median)</td>
<td>FMA</td>
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<td>Wu et al.</td>
<td>55±15.9</td>
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<td>Summerville et al.</td>
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<td>75±20±9</td>
<td>FMA</td>
</tr>
</tbody>
</table>

### Notes

- *p<0.05
- *p<0.01
- **p<0.001
- Not significant (p>0.05)
Three studies were included in the meta-analysis of total FIM scores (Figure 3).30,31,35 While the BAT group improved, on average 1.41 points on the FIM and the control group by 0.96 points, there was no significant improvement in total FIM scores (MD=0.454; SE=2.305; p=0.844).

Analysis 3: MAL AOU and QOM
Three studies were included30,31,34 in the analysis of the MAL (Figure 4). The BAT group improved by 0.47 points on the MAL-AOU and the control improved by 0.32 points; however, overall there was no significant improvement demonstrated (MD=0.150; SE= 0.176; p=0.494). On average the BAT group improved by 0.61 points on the MAL-QOM whereas the control improved by 0.46 points. Similarly, MAL QOM scores also did not improve significantly (MD=0.154; SE= 0.195; p=0.431).

Analysis 4: MAS
Two studies included MAS36,37 in their analysis and only the total scores were examined (Figure 5). MAS total scores reported no significant improvement (MD=0.658; SE=1.023; p=0.520) despite an average improvement by the BAT group of 0.95 points and by the control group, 0.29 points.

Discussion
This systematic review included eight RCTs that compared the effect of BAT versus standard rehabilitation on upper limb functioning and activities of daily living among chronic stroke survivors. Although multiple studies have shown BAT as a viable stroke rehabilitation technique13,14,18,30-34,36,38,39, the findings
Bilateral Arm Training in Stroke

**Figure 4.** Meta-analysis of three studies examining the Motor Assessment Log amount of use (AOU) and quality of movement (QOM)

<table>
<thead>
<tr>
<th>Studyname</th>
<th>Statistics for each study</th>
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<td>Standard error</td>
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<tr>
<td>Wu et al., 2011</td>
<td>0.120</td>
<td>0.271</td>
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</table>

Control BAT

**Figure 5.** Meta-analysis of two studies examining the Motor Assessment Scale

<table>
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<th>Studyname</th>
<th>Statistics for each study</th>
<th>Difference in means and 95% CI</th>
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<td>Difference in means</td>
<td>Standard error</td>
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<tr>
<td>Wu et al., 2011</td>
<td>0.190</td>
<td>0.316</td>
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</table>

Control BAT

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from all but one outcome measure, FMA, indicated that BAT showed a general trend in improvement over standard therapy, although it was not statistically significant. This finding has been supported by previous meta-analyses and systematic reviews examining BAT at all stages of stroke recovery.38

Individually, the included studies were generally underpowered to detect significant differences between groups due to their small sample sizes. The claims made were overly positive with wide confidence intervals for treatment effect. The current meta-analysis adds to the body of literature by combining multiple study samples in an attempt to remove statistical error to report accurate relationships between BAT and upper limb recovery. Thus, the pooled sample in this meta-analysis allows for a more accurate assessment of BAT’s role in upper limb recovery. Additionally, considering that individuals who are ≥6 months post-stroke experience different needs than those in earlier phases of recovery, this review adds knowledge to the existing gap in stroke rehabilitation literature as it specifically examined BAT during the chronic phase. A previous Cochrane review39 was published in 2010 but all patients were included in the analysis without consideration for time since stroke; that is, patients in the acute, sub-acute, and chronic phase of stroke grouped together and analyzed.

Stroke survivors are not only interested in motor functioning, but activities of daily living and quality of life outcomes as well. Interestingly, neither motor function nor activities of daily living (FIM) was found to improve with BAT; this finding is consistent with the Cochrane review as well.39 It has been reported that the FIM is not suited to ongoing, long-term assessment in the community-based setting.40 Given that the included subjects were in the chronic phase, the FIM was administered in a community-based setting, not a hospital or in-patient rehabilitation setting. These chronic patients are in a unique phase of stroke recovery whereby the FIM alone may not capture subtle changes in daily functioning. In addition to the FIM, quality of life measures that examine subjective health and wellbeing are an extremely important outcome to assess that should be considered for future studies.

It is important to note that the average age of a stroke patient in Canada is 69 years old and prevalence increases with age.41 Studies included in this analysis were, on average, much younger than the typical stroke patient, reporting a mean age of 51.4 years and a median of 57.4 years. This discrepancy could be due to the increasing number of strokes affecting more young persons as all eight of the studies included in the analysis were published within the last ten years and six in the last five years. The reasons for this trend could be a rise in risk factors such as diabetes, obesity, and high cholesterol as well as improved diagnostic methods for the identification of younger stroke sufferers. Future studies should consider examining BAT among those who suffered a stroke at varying ages.

It is possible that BAT has not been shown to be significantly more beneficial in improving upper limb recovery compared to standard therapy due to the low intensity with which it is provided. To elicit a significant neuroplastic change in behaviour, high numbers of repetitions of task-specific activity are crucial. Animal studies in neuroplasticity have shown that 400 to 600 repetitions per day of challenging fine-motor exercises are required to promote significant structural neurological changes following stroke.42 Thus, future studies should aim to better determine the effects of varying levels of BAT intensity on outcomes. At present, BAT is a low-intensity training regime which, although advantageous as it can appeal to a wide post-stroke audience, may come at a cost of slower recovery. Examining intensity effects could aid in our understanding of specific treatment regimens and protocols for unique stages of stroke recovery. It may also be beneficial to examine the combined effects of BAT and UAT in sequence to further understand the differences, similarities, or additive advantage of the two therapies. Future trials should include large, homogenous samples that receive varying intensities of BAT over a longer period of time.

It is important to note an important limitation associated with this study. A mean time since stroke of ≥6 months was chosen to allow the greatest number of studies to be eligible for inclusion; setting the minimum cut-off for all subjects would have limited the pool of studies with which to choose from. Based on the mean, subjects may be in either the acute or subacute phase, and consequently induce some amount of variability into the results.

Conclusion
Our results, along with the associated literature, demonstrate that BAT showed a general trend in improvement over standard therapy, although it was not statistically significant. This suggests that therapists have another tool available for upper limb rehabilitation and that, at minimum, it is as effective as normal standard of care. It should be noted that there was great variability in methodology, sample size, and
outcomes measures used among the studies included. We suggest that future studies improve methodological quality by implementing strict inclusion/exclusion criteria, controlling for confounders, standardizing BAT protocols, and recruiting a suitable sample size.

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system. Canadian Medical Association Journal, 164(13), 1853-1855.