Complex Traditional Chinese Medicine for Poststroke Motor Dysfunction
A Systematic Review

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Background and Purpose—For its current dimensions, stroke represents the world’s primary health challenge. In China stroke is the second most common cause of death. Traditional Chinese Medicine (TCM) has for many centuries been used, and it is still widely used today in countries of south and east Asia for the treatment of people with stroke. The objective of this systematic review was to evaluate whether complex Traditional Chinese Medicine (cTCM) improves poststroke motor recovery. In particular, we defined cTCM as intervention that included at least acupuncture and Chinese herbal medicine.

Methods—An extensive search including PubMed, EMBASE, CBM, and the Cochrane Library was performed up to December 2007. Randomized clinical trials (RCTs) about cTCM for motor dysfunction of poststroke were searched irrespective of any language. The quality of each trial was assessed according to the Cochrane Reviewers’ Handbook 4.2.6.

Results—After selection of 11 234 articles, 34 RCTs and quasi-RCTs were included. All these trials were conducted in China and published on Chinese journals. All trials but one reported results in favor of cTCM treatments suggesting a strong publication bias. Because of the significant clinical and methodological heterogeneity, no meta-analysis was performed and thus no cumulative result was obtained pooling data of RCTs.

Conclusions—What appears from this systematic review is that scant data are available to evaluate efficacy of cTCM for poststroke motor dysfunction. Most of the primary studies available for this review were inadequately designed trials characterized by unknown dropout rates and definitional vagueness in outcomes measures. None of the studies approached important end points like death, survival times, rate of dependency, reduction in length of stay in hospital, etc. The key to lead to evidence-based practices is establishing a consensus on standardized relevant outcome measures and then designing and conducting appropriate RCTs that adopt those standards.

Key Words: traditional Chinese medicine • systematic review • stroke • rehabilitation

Annually, 15 million people worldwide suffer from stroke. Of these, 5 million die and another 5 million are left permanently disabled. Stroke is the biggest single cause of major disability. As such, stroke represents a heavy burden both on family and community.¹

In China official statistics data show that stroke is the second most common cause of death among both urban and rural residents (117 per 100 000 per year in cities, and 112 per 100 000 in rural populations). The age-adjusted stroke prevalence in China varies from 259 per 100 000 to 719 per 100 000 for all ages.²

Traditional Chinese Medicine (TCM) has for many centuries been used, and it is still widely used today in countries of south and east Asia for the treatment of people with stroke. With the purpose of investigating the appropriate scientific evidence for TCM the Italian National Institute of Health and the Tianjin University of Traditional Chinese Medicine have implemented a common project, the Joint Sino-Italian Laboratory (JoSIL) on TCM. This systematic review was conducted within the framework of JoSIL.

Many systematic reviews of Chinese traditional treatments in stroke rehabilitation have been published, mainly on Chinese journals. Some systematic reviews were delivered by the Cochrane Library, mainly related to the acute phase of stroke. Most of these studies investigated the role of acupuncture or Chinese herbal medicines alone with contradictory conclusions.³–⁶ TCM includes acupuncture, massage, physical exercise, and Chinese herbal medicines, which are usually used in combination in clinical practice. However, whether or not the combinations of these treatments are truly effective...
Methods

Types of Studies
Randomized and quasirandomized clinical trials to evaluate cTCM for poststroke interventions up to December 2007 were searched irrespective of language. Quality-RCTs are trials that use approaches to allocate patients, such as alternation, case record numbers, birth date, etc. These methods of allocation are relatively easy to manipulate, introducing selection bias.

Types of Participants
Trials including patients with ischemic or hemorrhagic stroke of any age or sex were eligible. Stroke had to be diagnosed according to the World Health Organization definition or to the corresponding diagnostic criteria adopted in China, or confirmed by computerized tomography or MRI. Trials that included patients in an acute phase (within 10 days from onset) were excluded. The reason for this choice depends on the fact that we wanted to investigate the effectiveness of cTCM on motor function in the rehabilitation stage and not in the acute phase. In the acute phase the patients are at high risk and their treatment should comply, also in China, with the International guidelines. A 10-day interval from the onset was adopted in some clinical trials to distinguish the acute/non acute stroke phase (eg, http://clinicaltrials.gov/ct2/show/NCT00849303). Trials of patients with subarachnoid hemorrhage and subdural hematoma were not considered.

Types of Interventions
We included in our review only trials that included at least acupuncture and some kind of herbal medicine. Either traditional acupuncture in which the needles were inserted in classical meridian points or acupuncture in which the needles were inserted in non-meridian or trigger points were considered, regardless of the source of stimulation (for example, manual or electric stimulation). “Injectio ad acumen” acupuncture was also included, this technique consists of injecting Chinese medicine into certain acupoints. All the preparations of different Chinese herbs or extractions were considered. All studies were required to have treatment duration of at least 1 week.

Types of Outcome Measures
All the trials concerning the patients and the treatments previously described were considered eligible for our review independently from the outcomes studied (death, activities of daily living [ADL], functional recovery, quality of life [QoL], etc.).

Study Selection
To identify all relevant articles, a comprehensive search was performed in December 2007. We searched the Cochrane Central Register of Controlled Trials (2008, issue 1), PubMed (1950–2007), EMBASE (1980–2007), and the Chinese Biomedical Database (1978–2007). We also searched other Chinese journal databases (Chinese Journal Full-Text Database and Scientific Journal Database) to identify thesis and conference articles. The search terms used were “traditional Chinese medicine, acupuncture, massage, scraping, ventouse, acupoint, complex therapy” and “stroke, apoplexy, brain infarction, cerebral infarction, hematencphalohemorrhage.”

These terms were used as free-text terms (translated to Chinese) to search some of the Chinese databases, Free-text and MeSH terms were used to search CBM, PubMed, and Cochrane Library. Free-text and Emtree terms were used to search EMBASE.

We also examined the bibliographies of all of the considered publications so as to identify other studies. Two reviewers (Zhang Junhua and Shang Hongcai) independently examined titles and abstracts of the trials for inclusion, based on the selection criteria outlined above. A table with the English translation of all the titles and a summary of the articles was prepared and reviewed by a third investigator (Francesca Menniti-Ippolito). The full texts of articles were retrieved if there was any doubt whether an article should be excluded or not. Inconsistencies were solved through discussion. The selected trials that were claimed to be randomized were retrieved and then examined for confirmation that they were indeed correctly randomized.

Quality Assessment of Trials Included
A quality assessment was carried out for all the retrieved studies. Quality in a systematic review refers essentially to the absence of biases.

The main biases in a clinical trial can derive from systematic differences between comparison groups in: measured or unmeasured baseline characteristics because of the way participants were selected or assigned (selection bias), care provided apart from the intervention being evaluated (performance bias), how outcomes are ascertained, diagnosed or verified (detection bias), withdrawals or exclusions of participants from the results of a study (attrition bias).

To assess the methodological validity of the studies included in this review the following aspects were evaluated (according to a binary score presence/absence): randomization, allocation concealment, blinding, and description of follow-up. According to Cochrane reviewers’ Handbook 14 3 categories were defined: (1) all quality criteria met; (2) one or more of the quality criteria only partly met; (3) one or more criteria not met.

Articles were assessed by 2 reviewers (Zhang Junhua and Shang Hongcai) independently. Disagreements were resolved by consultation with a third reviewer (Gao Xiumei).

Data Extraction
The information on patients, methods, interventions, outcomes, and results was extracted and summarized by 4 reviewers (Zhang Junhua, Xiong Jun, Xu Yuanjuan, Zhang Xin) using a standardized data extraction form. Disagreements were resolved through discussion among all investigators. For dichotomous outcomes, the number of responders and the total number of participants for each study arm were extracted. For continuous outcomes (eg, deficit of neurological score), the mean change and standard deviation for the mean in each group of the trial were extracted along with the total number.

Data Analysis
In this study, statistical analysis was performed using software provided by the Cochrane Collaboration (Review Manager 5).

We did not perform any estimate of pooled effect because of clinical and methodological heterogeneity among the trials included in the review.

Results
Search Flow
An initial screening yielded 11 235 potentially relevant citations in accordance with the search strategy. According to the inclusion criteria, on the basis of the titles and abstracts, 11 166 articles were excluded. These studies were mainly excluded because duplicates of the same articles included in different databases, because the tested treatments were not cTCM, or because they were not RCTs. After the full text reading of 69 articles, 35 studies were further excluded mainly because they had included patients in the acute phase of stroke. Ultimately, 34 studies were included for analysis (see Figure 1). All of the trials were conducted in China and published on Chinese journals in Chinese language (only 3 papers had an English abstract). All the included studies were for stroke is still unknown. The objective of our systematic review was to determine whether complex TCM treatments (cTCM) improves poststroke motor recovery. In particular, we defined cTCM as intervention that included at least acupuncture and Chinese herbal medicine.
single-center, parallel-design and claimed to have applied randomization.

**Characteristics of the Trials Included in the Systematic Review**

The main characteristics of the 34 trials are presented in Table 1. The number of participants included in each of the studies ranged from 39 to 398, with a total of 4521 patients (2403 patients in the investigational groups) in the 34 studies. The proportion of males was approximately 61.5%. The age of the participants ranged from 35 years to 92 years. Eleven of the trials included patients with ischemic stroke only, and the remaining included patients with ischemic and hemorrhagic stroke. The time from stroke onset to the inclusion in the trial ranged from 12 days to 6 years. In 27 of the trials diagnostic criteria for stroke were specified, and in 20 inclusion criteria were defined. Only 8 trials reported a complete description of all selection criteria for the subjects (eg, diagnosis, inclusion, exclusion criteria). The baseline characteristics of the participants were available for 26 studies.

Almost all trials, but 6, adopted a design in which patients were allocated to receive either control treatments or control treatments plus experimental treatments (A+B versus B design).

We classified the trials according to the control group treatments in 4 different groups: acupuncture alone (with or without physical exercise); Chinese herbal medicine alone; Western medicine (with or without any other Chinese treatment or physical exercise); physical exercise. The duration of therapy ranged from 10 days to 3 months.

There was only 1 placebo-controlled study (placebo defined as starch capsules + decoction of Henon Bamboo leaf + sham acupuncture). The most tested herbal preparation was Buyanghuanwu decoction (8 of the trials). Buyanghuanwu is a traditional Chinese prescription for decoction that has been used clinically to treat paralysis in China for hundreds of years. The decoction contains earth worms and 6 medicinal herbs as raw material without any extraction or standardization: Huang Qi (Radix Astragali), Dang Gui (Radix Angelicae Sinensis), Chuan Xiong (Rhizoma Chuanxiong), Chi Shao (Radix Paeoniae Rubrae), Tao Ren (Semem Persicae), Hong Hua (Flos Carthami Tinctoori). Another frequently tested preparation was Mailuoling, administered as injection, made by extracting herbal Shi Hu (Herba Dendrobii), Xuan Shen (Radix Scrophularia), Jin Yin Hua (Flos Lonicerae), and Niu Xi (Radix Achyranthis Bidentatae). The most commonly used acupoints are listed in Table 2.

A variety of outcome measures were reported. No data on death or dependency at the end of follow-up were available in any of the trials included. The “Effective Rate” (ER) was the most commonly used measure to evaluate efficacy (used in 29 of the trials). This measure is extensively cited in Chinese biomedical literature to define the proportion of responders to treatments or interventions. For poststroke treatments a “responder” was defined on the basis of a combined evaluation of muscle strength, and functional independence measure (FIM) or activities of daily living (Barthel ADL Index). Two of the trials used the Fugl-Meyer motor function assessment as an index. Two of the trials used the FIM as an index. Only 1 trial reported the neurological deficit score. Other outcome measures are indicated in Table 1. Adverse events were reported in 1 trial only.

**Methodological Quality**

All the included studies indicated randomization, with only 2 of the trials reporting that the random sequence was generated by a random digits table. Three trials allocated patients by the sequence of admission. No trial described allocation concealment or mentioned blinding procedures. None of the trials described withdrawal and intention-to-treat analyses. Only 1 of the trials reported data on follow-up observations. In general, the methodological quality of the trials included was poor. According to the Cochrane handbook, all of the trials included were of low quality classified as “C”.

**Effectiveness**

Almost all the trials (29/34) used the ER as an outcome measure. For these studies an “effective rate ratio” (ERR) was calculated as the ratio between the proportion of responders in the treatment group and the proportion of responders in the control group. All trials but 1 reported ERR in favor of cTCM treatments (in 15 trials the ERR was statistically significant). The results of the studies using the ERR measure are reported in the forest plot in Figure 2.

A strong publication bias is present in our review as can be seen by the asymmetry of the funnel plot reported in Figure 3. Five trials used only continuous outcomes (eg, deficit of neurological score), in these the mean change and standard deviation for the mean were considered as effectiveness measures.

**cTCMs Versus Acupuncture**

As illustrated in Figure 2, 4 of the 12 trials of cTCM versus acupuncture alone showed statistically significant higher ERR after treatment with the cTCM. These results can be summarized as: Buyanghuanwu decoction plus acupuncture was more effective than acupuncture alone (ERR, 1.37: 95% CI, 1.02 to 1.85); a mixed powder of Panax pseudo-Ginseng and Lecith and Lecithin (Sanqi and Shuizhi) plus acupuncture was more effective than acupuncture alone (ERR, 1.38: 95% CI, 1.06 to 1.80); Jinmaikangfu decoction plus acupuncture was more effective than acupuncture alone (ERR, 1.57: 95% CI, 1.18 to 1.85); Mailuoling injection plus acupuncture was more effective than acupuncture alone (ERR, 1.38: 95% CI, 1.02 to 1.85).
<table>
<thead>
<tr>
<th>Study (Ref No.)</th>
<th>Type</th>
<th>TO</th>
<th>T C</th>
<th>Treatment to be Tested</th>
<th>Allocated Arm</th>
<th>Control Arm</th>
<th>Outcome Measures</th>
<th>Treatment Duration</th>
<th>Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tang 1993(^{16})</td>
<td>Ci/H</td>
<td>2 w to 6 m</td>
<td>121 40</td>
<td>Acup + herbal medicine + bath + i-acum</td>
<td>TT + PE</td>
<td>PE + placebo (Decoction of Henon Bamboo Leaf + starch capsules + Sham Acup)</td>
<td>ER, Japanese ADL scale, Hemorheology test</td>
<td>60 days</td>
<td>4</td>
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<tr>
<td>Yang 1997(^{17})</td>
<td>Ci/H</td>
<td>&gt; 1 m</td>
<td>146 108</td>
<td>Maluoluling injection</td>
<td>TT + Acup</td>
<td>Acup</td>
<td>ER</td>
<td>30 days</td>
<td>1</td>
</tr>
<tr>
<td>Zhu 1998(^{18})</td>
<td>Ci/H</td>
<td>2 w to 6 m</td>
<td>32 31</td>
<td>Acup</td>
<td>TT + Yiqihuayu decoction</td>
<td>Yiqihuayu decoction</td>
<td>ER</td>
<td>20 days to 60 days</td>
<td>2</td>
</tr>
<tr>
<td>Tian 1999(^{19})</td>
<td>Ci/H</td>
<td>...</td>
<td>21 18</td>
<td>Electro Acup</td>
<td>TT + Buyanghuanwu decoction</td>
<td>Buyanghuanwu decoction</td>
<td>Recovery time of speech and sensory function</td>
<td>1 m</td>
<td>2</td>
</tr>
<tr>
<td>Li 2000(^{20})</td>
<td>Ci</td>
<td>1 to 15 m</td>
<td>60 50</td>
<td>Huoiaotang</td>
<td>TT + Acup + PE</td>
<td>Acup + PE</td>
<td>ER</td>
<td>15 days</td>
<td>1</td>
</tr>
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<td>Ci/H</td>
<td>...</td>
<td>200 198</td>
<td>Acup</td>
<td>TT + Buyanghuanwu decoction</td>
<td>Buyanghuanwu decoction</td>
<td>ER</td>
<td>30 days</td>
<td>2</td>
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<td>...</td>
<td>155 60</td>
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<td>herbal medicine</td>
<td>ER</td>
<td>10 days</td>
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</tr>
<tr>
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<td>Ci/H</td>
<td>...</td>
<td>165 60</td>
<td>Acup</td>
<td>TT + Acup</td>
<td>Acup</td>
<td>ER</td>
<td>20 days</td>
<td>1</td>
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<td>Ci/H</td>
<td>...</td>
<td>183 183</td>
<td>Acup</td>
<td>TT + Huoiaotuzaizhao bolus + herbal medicine</td>
<td>Huoiaotuzaizhao bolus + herbal medicine</td>
<td>ER, muscle strength</td>
<td>10 days</td>
<td>2</td>
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<td>...</td>
<td>48 52</td>
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<td>TT + Maluoluling + piracetam + nicholin</td>
<td>Maluoluling + piracetam + nicholin</td>
<td>ER</td>
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<td>34 26</td>
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<td>herbal medicine</td>
<td>ER</td>
<td>2 m</td>
<td>2</td>
</tr>
<tr>
<td>Li 2002(^{27})</td>
<td>Ci/H</td>
<td>...</td>
<td>35 30</td>
<td>Acup</td>
<td>TT + Acup</td>
<td>Acup</td>
<td>ER</td>
<td>30 days</td>
<td>3</td>
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<tr>
<td>Shao 2002(^{28})</td>
<td>Ci</td>
<td>1 m to 6 y</td>
<td>25 23</td>
<td>Acup</td>
<td>TT + Buyanghuanwu decoction</td>
<td>Buyanghuanwu decoction</td>
<td>ER, symptom score</td>
<td>10 days</td>
<td>2</td>
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<tr>
<td>Wang 2002(^{29})</td>
<td>Ci/H</td>
<td>1 m to 3 y</td>
<td>82 46</td>
<td>Acup + herbal medicine</td>
<td>TT</td>
<td>Acup</td>
<td>ER</td>
<td>2 m</td>
<td>1</td>
</tr>
<tr>
<td>Wang-J 2002(^{30})</td>
<td>Ci</td>
<td>15 days to 6 m</td>
<td>68 44</td>
<td>Acup + Tanfukang</td>
<td>TT + aspirin + troxerutin + cerebrolysin + PE</td>
<td>aspirin + troxerutin + cerebrolysin + PE</td>
<td>Muscle strength and physical activity, Hemorheology test</td>
<td>4 w</td>
<td>3</td>
</tr>
<tr>
<td>Wang-G 2003(^{31})</td>
<td>Ci/H</td>
<td>1 m to 1 y</td>
<td>38 32</td>
<td>Acup + Buyanghuanwu decoction</td>
<td>TT + PE</td>
<td>PE + Compound Danshen tablet + piracetam + vitaE</td>
<td>ER</td>
<td>2 w</td>
<td>2</td>
</tr>
<tr>
<td>Liu 2003(^{32})</td>
<td>Ci</td>
<td>...</td>
<td>80 76</td>
<td>Liguistrazine</td>
<td>TT + Acup + vitaE + ATP + recognan</td>
<td>Acup + vitaE + ATP + recognan</td>
<td>ER</td>
<td>1 m</td>
<td>3</td>
</tr>
<tr>
<td>Liu-YP 2003(^{33})</td>
<td>Ci</td>
<td>2 to 4 w</td>
<td>60 60</td>
<td>Electro Acup + Buyanghuanwu decoction</td>
<td>TT</td>
<td>Tengxinluo capsule</td>
<td>ER</td>
<td>2 w</td>
<td>2</td>
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<td>Ci</td>
<td>...</td>
<td>25 23</td>
<td>Acup</td>
<td>TT + Buyanghuanwu decoction</td>
<td>Buyanghuanwu decoction</td>
<td>ER</td>
<td>10 days</td>
<td>2</td>
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<tr>
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<td>&gt; 6 m</td>
<td>20</td>
<td>Buyanghuanwu decoction</td>
<td>TT + Acup</td>
<td>Acup</td>
<td>ER, physical activity</td>
<td>30 days</td>
<td>2</td>
</tr>
<tr>
<td>Liu 2004(^{36})</td>
<td>Ci/H</td>
<td>...</td>
<td>60 60</td>
<td>Acup + Simiaoyongan decoction</td>
<td>TT</td>
<td>Buyanghuanwu decoction</td>
<td>FMA, FIM</td>
<td>30 days</td>
<td>2</td>
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<td>6 to 12 m</td>
<td>43 43</td>
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<td>TT + Acup</td>
<td>Acup</td>
<td>ER</td>
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<td>Lai 2005(^{38})</td>
<td>Ci/H</td>
<td>...</td>
<td>33 35</td>
<td>Powder of Sanqi and Shuizhi</td>
<td>TT + Acup</td>
<td>Acup</td>
<td>ER</td>
<td>15 days</td>
<td>1</td>
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</table>

(Continued)
Table 1. Continued

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<tr>
<th>Study (Ref No.)</th>
<th>Type</th>
<th>T0</th>
<th>T</th>
<th>C</th>
<th>Treated Arm (TT)</th>
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<th>Outcome Measures</th>
<th>Treatment Duration</th>
<th>Group</th>
</tr>
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<td>Ci/H</td>
<td>2 w to 6 m</td>
<td>30</td>
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<td>Acup</td>
<td>ER</td>
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</tr>
<tr>
<td>Xu 200560</td>
<td>Ci</td>
<td>. . .</td>
<td>36</td>
<td>35</td>
<td>Electro Acup</td>
<td>TT + Naogengling + Xuesaitong + recognogn + dextran</td>
<td>Naogengling + Xuesaitong + recognogn + dextran</td>
<td>ER</td>
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</tr>
<tr>
<td>Li 200661</td>
<td>Ci/H</td>
<td>≤ 6 m</td>
<td>119</td>
<td>58</td>
<td>Acup + herbal medicine + massage + bath</td>
<td>TT + PE</td>
<td>PE</td>
<td>FMA, Barthel ADL index</td>
<td>4 w</td>
</tr>
<tr>
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<td>Ci/H</td>
<td>1 to 12 m</td>
<td>54</td>
<td>61</td>
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<td>Acup + i-acum</td>
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<td>15 days x 2</td>
</tr>
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<td>Wu 200663</td>
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<td>1 to 15 m</td>
<td>60</td>
<td>51</td>
<td>Acup + massage</td>
<td>TT + PE + Xuesaitong + CTP</td>
<td>PE + Xuesaitong + CTP</td>
<td>ER</td>
<td>30 days x 2</td>
</tr>
<tr>
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<td>Ci</td>
<td>12 days to 6 m</td>
<td>39</td>
<td>39</td>
<td>Acup</td>
<td>TT + Buyanghuanwu decoction + Xuesaitong</td>
<td>Buyanghuanwu decoction + Xuesaitong</td>
<td>ER</td>
<td>15 days x 3</td>
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<tr>
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<td>2 to 4 w</td>
<td>40</td>
<td>37</td>
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<td>TT</td>
<td>aspirin + high pressure oxygen</td>
<td>ER</td>
<td>10 days x 3</td>
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<tr>
<td>Peng 200746</td>
<td>Ci . . .</td>
<td>30</td>
<td>30</td>
<td>Acup + PE</td>
<td>TT + Buyanghuanwu decoction</td>
<td>Buyanghuanwu decoction</td>
<td>ER</td>
<td>15 days x 2</td>
<td>2</td>
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<tr>
<td>Sun 200747</td>
<td>Ci/H</td>
<td>. . .</td>
<td>32</td>
<td>32</td>
<td>Buyanghuanwu decoction</td>
<td>TT + Acup</td>
<td>Acup</td>
<td>ER</td>
<td>Haemorheology test</td>
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<tr>
<td>Yang 200748</td>
<td>Ci/H</td>
<td>&lt; 12 m</td>
<td>50</td>
<td>50</td>
<td>Acup + Yindan Xinaotong capsule</td>
<td>TT</td>
<td>Danshen injection</td>
<td>ER, FIM</td>
<td>2 m</td>
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<tr>
<td>Zhang 200749</td>
<td>Ci</td>
<td>3 m to 1 y</td>
<td>56</td>
<td>50</td>
<td>Acup + Buyanghuanwu decoction</td>
<td>TT + cerebrolysin + aspirin</td>
<td>cerebrolysin + aspirin</td>
<td>Neurological Deficit Score, Haemorheology test</td>
<td>3 w</td>
</tr>
</tbody>
</table>

Group indicates type of control treatment: (1) Acupuncture; (2) Herbal Medicine; (3) Western Medicine; (4) Physical Exercise.
T0 indicates time since onset of stroke; T/C, No. of patients treated per control arm; Ci, cerebral infarction; Ci/H, cerebral infarction and cerebral hemorrhage; Acup, acupuncture; PE, physical exercise; i-acum, injection ad acumen; ER, effective rate; FMA, Fugl-Meyer assessment; ADL, activities of daily living; FIM, functional independence measure.

effective than acupuncture alone (ERR, 1.11; 95% CI, 1.03 to 1.20).17 The remaining 8 trials did not show statistically significant differences between the experimental and control groups.

In 2 other trials the control group included acupuncture plus physical exercise. Only 1 showed a statistically significant result: Huonaotang decoction, acupuncture, and physical exercise was more effective than physical exercise plus acupuncture (ERR, 1.16; 95% CI, 1.04 to 1.31).20

cTCMs Versus Herbal Medicine

Five of 12 trials showed statistically significant higher ERR after treatment with the cTCMs as compared to herbal medicine alone. These results can be summarized as: Buyanghuanwu decoction plus acupuncture was more effective than Buyanghuanwu decoction alone in 3 trials21,28,34; treatment with herbal medicine prescribed on the basis of individual symptoms and signs plus common and head acupuncture was more effective than herbal medicines (ERR, 1.23; 95% CI, 1.08 to 1.39)22; Yindan Xinaotong capsule plus acupuncture was more effective than Danshen injection (ERR, 1.21; 95% CI, 1.02 to 1.42).48 This study reported also a statistically significant result on activities of daily living using FIM (WMD, 8.42; 95% CI, 5.85 to 10.99), but not on neurological deficit.

Activities of daily living and effects of motor function were investigated respectively with FIM the Fugl-Meyer scale in a study on acupuncture plus Simiaoyongan decoction and Buyanghuanwu decoction. Acupuncture plus Simiaoyongan decoction was more effective than Buyanghuanwu decoction (WMD, 26.2; 95% CI, 18.56 to 33.84).36

cTCMs Versus Western Medicines (With or Without Chinese Treatments)

Four of 7 trials showed statistically significant higher ERRs after treatment with the cTCMs compared to Western medicine (with or without Chinese treatments). These results can

Table 2. Commonly Used Acupoints in Included Studies

<table>
<thead>
<tr>
<th>Site</th>
<th>Chinese Name of Acupoints</th>
<th>International Standard Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head</td>
<td>Dicang, jiache, lianquan, and fengchi</td>
<td>ST-4, ST-6, CV-23, and GB-20</td>
</tr>
<tr>
<td>Upper limbs</td>
<td>Jianyu, quchi, hegu, shousanli, waiguan, and neiqian</td>
<td>LI-15, LI-11, LI-4, LI-10, TE-5, and PC-6</td>
</tr>
<tr>
<td>Lower limbs</td>
<td>Zusanli, yanglingqian, huantiao, taichong, jiezi, kunlun, sanyinjiao, and fengshi.</td>
<td>ST-36, GB-34, GB-30, LR-3, ST-41, BL-60, SP-6, and GB-31</td>
</tr>
</tbody>
</table>
be summarized as: Dihuang Yinzi plus acupuncture was more effective than aspirin plus high pressure oxygen (ERR, 1.53; 95% CI, 1.10 to 2.12); Yiqi huoxue medicine plus acupuncture was more effective than piracetam (ERR, 1.18; 95% CI, 1.03 to 1.35); Buyang huawu decoction plus acupuncture and rehabilitation exercise was more effective than piracetam plus vitamin E and compound Danshen tablets (ERR, 1.32; 95% CI, 1.05 to 1.66); acupuncture, massage, physical exercise and Xesaitong plus cytidine triphosphate (CTP) was more effective than physical exercise and Xesaitong plus CTP (ERR, 1.15; 95% CI, 1.01 to 1.30).

**cTCMs Versus Physical Exercise**

Treatment with herbal medicines based on symptoms and signs plus acupuncture, bath, *injectio ad acumen*, and rehabilitation exercise was more effective than placebo (defined...
as starch capsules + decoction of Henon Bamboo leaf + sham acupuncture) plus physical exercise (ERR, 2.04; 95% CI, 1.47 to 2.82).16

Adverse Events
Only 1 study reported adverse events: 5 patients in the cTCMs group of 121 patients had mild stomach discomfort.16

Discussion
One of the most important aspects of our review refers to the methodological approach adopted in the studies. In our systematic review, in fact, it was not possible to find well-designed trials to evaluate efficacy of complex TCM treatments for the management of poststroke motor dysfunction. Most of the trials included in this review used an “A + B versus B” design where patients are randomized to receive a control treatment (the Control Group) versus a control treatment plus the experimental treatment (the Treatment Group). This kind of design is quite popular in acupuncture studies where acupuncture is added to usual care; nevertheless, it is likely to generate false-positive results. Without a rigorous control for placebo effect, by using nonpenetrating or sham devices or placebo herbal medicine in the control group, the results of these studies would be positive because of nonspecific-placebo effects related to the additional care given to patients in the treatment group, or by the disappointment experienced by patients of the control group, when not receiving the experimental treatments they may have hoped for.50

Because of the significant clinical heterogeneity (eg, different interventions, different time since stroke onset), it was not possible to perform a pooling analysis of the trials. Fourteen trials did not define the time to onset of stroke, and 11 trials included patients with long intervals to stroke onset (from 12 days to 6 years). This can affect the external validity of the studies (ie, the extent to which the observed effects could be generalized in the clinical practice).

With regard to the quality of reporting of the trials a common shortcoming was the inadequate description of the randomization and blinding procedures. A large number of these trials actually claimed to be RCTs, but most of the authors have apparently misunderstood the full concept of randomization. Allocation concealment was not reported in any of the trials included. Other important weaknesses were the very poor descriptions of dropouts and of harm-related issues (none of the trials reported patient withdrawals, and only 1 study described the occurrence of adverse events).

As far as the herbal medicines are concerned, quality control of herbal preparations is not mentioned in trial reports, although this is crucial for the validity of the study results. To assess the efficacy of a specific product in a clinical study, all participants should be given exactly the same intervention in terms of product identity, purity, dosage, and formulation.

Overall, because of the poor methodological qualities of the studies, the results of the trials included in this systematic review are likely to be biased by many factors. Furthermore, because the review included only articles published on the Chinese literature, a location bias cannot be excluded (ie, trials published in low or nonimpact factor journals are more likely to report significant results than those published in high-impact mainstream medical journals) as demonstrated by the asymmetry of the funnel plot shown in Figure 3.

Also other systematic reviews of TCM had encountered similar problems, and the Chinese Government is stimulating, through huge investments, the improvement of the studies aiming to prove the efficacy of Chinese medicine according to International standards. In our review only 2 of the 34 selected articles declared the source of funding.

A critical element in conducting systematic reviews is having access to all relevant publications that address the clinical question. There is the possibility that in our review we were not able to identify all relevant studies. Important results may have been published in reports, technical reports, discussion papers or other formats which were not indexed in the databases we used. Comprehensive identification of such “gray literature” is hard to achieve. Another possible limitation of our review is that we did not have the opportunity to contact study authors for obtaining additional information about the included studies.

The primary studies available for this review were mostly inadequately designed trials characterized by unknown dropout rates and definitional vagueness in outcomes measures.

None of the studies included in our review approached important end points like, for example, death, survival times, rate of dependency, reduction in length of stay in hospital or long term care institution, etc. All the trials were actually focused on ancillary or surrogate outcomes measured through subjective qualitative scores (ie, “notable,” “effective,” “ineffective,” etc). In all the trials the duration of therapy and follow-up was indeed too short to allow to achieve conclusive results on more relevant outcomes.

Both these aspects (the low clinical relevance and the methods adopted to measure the end points) demonstrate the need to approach with more rigorous tools the study of a possible role of TCM in stroke. The key to lead to evidence-based practices is in establishing a consensus on standardized relevant outcome measures and then designing and conducting appropriate RCTs that adopt those standards.

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Disclosures
None.
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