

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Effectiveness of interventions to improve hand motor function in individuals with moderate to severe stroke: a systematic review protocol
AUTHORS	Wang, Hewei; Arceo, Ray; Chen, Shugeng; Ding, Li; Jia, Jie; Yao, Jun

VERSION 1 – REVIEW

REVIEWER	Bichun Ouyang RUMC, US
REVIEW RETURNED	09-Jul-2019

GENERAL COMMENTS	This is a well written protocol for a systematic review. The investigators discussed all key components in a systematic review. My only concern, also mentioned by the investigators, is that this review will include trials with different interventions and outcome measures. So it will be difficult to combine the data and perform any meta-analysis from which conclusions may be drawn about the overall effect of the intervention. But the investigators can at least discuss what meta-analysis may be possible, say in some subgroups.
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REVIEWER	Mark McGlinchey Guy's and St Thomas' Hospital NHS Foundation Trust King's College London United Kingdom
REVIEW RETURNED	13-Jul-2019

GENERAL COMMENTS	<p>Thank you for the opportunity to review this protocol which addresses a very clinically relevant research question. I have provided comments in the attached document.</p> <p>Review Checklist</p> <p>2. Is the abstract accurate, balanced and complete?</p> <p>The authors provide an overview of the justification of the systematic review, methods and data analysis in the abstract. The authors could provide more details regarding some aspects of the methodology e.g. dates of electronic searches, inclusion of randomised controlled trials (this is only mentioned later in the abstract when discussing the assessment of risk of bias), justification for only performing a qualitative synthesis. The authors could also provide more clarity regarding which statements are strengths and which statements are limitations in the "Strengths and Limitations of this study" section.</p>
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	<p>13. Is the supplementary reporting complete (e.g. trial registration; funding details; CONSORT, STROBE or PRISMA checklist)? The authors have referred to using the PRISMA-P checklist to guide their review protocol, which is an appropriate checklist. Could the authors complete PRISMA-P checklist and attach it as a supplementary file?</p> <p>15. Is the standard of written English acceptable for publication? The standard of written English is currently not acceptable for publication. For example:</p> <ul style="list-style-type: none"> • there are errors in subject-verb agreement <ul style="list-style-type: none"> o “previous evidence for effective treatments that recovers hand function...” o “to identify interventions that has potential to effectively...” o “currently this cohort of stroke survivors are largely ignored for hand function rehabilitation” • there are omissions of the definite article when required and inclusions of the definite article when not required <ul style="list-style-type: none"> o “Generally, hemiparesis impacts the movement function of [the] hand and wrist more than [the] shoulder and elbow.” o “[The] Above features results in the abnormal involuntary coupling...” o “As we know, the hand movements play a core role in upper limb function...” o “The PT is defined as ‘services to individuals and populations to develop, maintain and restore maximum movement • there are misspellings of commonly used words <ul style="list-style-type: none"> o “trials” is spelled as “trails” in the Types of Study, Participants and Analyses if Subgroups or Subsets sections o “trunk” is spelled as “truck” in the Discussion section • there are sentences where words are used that reduced the clarity of the sentence: <ul style="list-style-type: none"> o “With the progress of rehabilitation science and tool development, results from small clinical trials have been available.” Do the authors mean that results from small clinical trial are now available thereby justifying the systematic review? o “Secondary outcome measures will include kinematic analysis of hand movement, possible improvements of quality of life and possible mental health improvements related to the practice of interventions”. Do the authors mean that they will possibly include outcomes measures pertaining to quality of life and mental health? o “To the best our knowledge, this is the first systematic review that attempts to sort out the hand rehabilitation approaches...” Do the authors mean that they will highlight certain hand rehabilitation approaches the many available hand rehabilitation approaches? Do the authors mean that they will divide the different hand rehabilitation approaches into different categories? <p>Specific Queries Eligibility Criteria Types of Studies The authors have stated they will only include RCTs published in English, but they have not justified why they will only include RCTs and they have not justified why they will only include studies published in English. This latter aspect has the risk of excluding RCTs completed in countries where English is not the main language or where articles are written in another language. For</p>
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	<p>example, a recent Cochrane review by Pollock et al. and published in 2014 (Physical rehabilitation approaches for the recovery of function and mobility following stroke) included 96 studies, over half of which were carried out in China. As there was a need to translate articles written in Chinese, this would suggest that there may be potentially eligible articles that may be excluded by the proposed search strategy.</p> <p>Participants The authors have included scores on functional assessments to identify patients with moderate to severe unilateral hand dysfunction (Fugl-Meyer UE scale, Chedoke-McMaster Stroke Assessment) but they have not referenced the scores to indicate that they can be used to identify eligible participants. The authors should include references to justify these scores as indicators of severity of hand dysfunction.</p> <p>Types of Interventions The authors have stated that they will select all trials assessing a rehabilitation method- PT and OT. It is not usual to describe physical therapy/physiotherapy and occupational therapy as rehabilitation methods. They may be considered as interventions which in themselves encompass many different, individual interventions, such as exercise therapy, manual techniques, task-specific practice and education. Will the authors just include RCTs investigating the effects of “physiotherapy” or “occupational therapy” as a package of care, or will they include RCTs investigating the effect of individual interventions, such as CIMT or FES?</p> <p>Search Strategy for the identification of relevant studies The authors have included an example of a search strategy to be used for the systematic review, which seems quite brief. Whilst this may be due to the design of the Cochrane Library Database, it does not include the main interventions that the authors have identified (physical therapy/physiotherapy and occupational therapy). Could the authors include a more detailed search strategy?</p> <p>Strategy for Data Synthesis The authors have stated that they will provide a qualitative synthesis to summarise the main results. They state later that they anticipate that there will be limited scope for a meta-analysis due to the range of different outcome measures and heterogeneity of interventions across the existing trials based on initial screening. However, unless they have completed the data extraction process of the eligible studies (in which case it might be too late to publish the protocol), they cannot know for certain if they will not be able to do a meta-analysis, which is the more common method of presenting results from systematic reviews investigating the effectiveness of health care interventions. The authors should justify their strategy more clearly.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Bichun Ouyang

Institution and Country: RUMC, US

Comments to the Author :

1) This is a well written protocol for a systematic review. The investigators discussed all key components in a systematic review. My only concern, also mentioned by the investigators, is that this review will include trials with different interventions and outcome measures. So it will be difficult to combine the data and perform any meta-analysis from which conclusions may be drawn about the overall effect of the intervention. But the investigators can at least discuss what meta-analysis may be possible, say in some subgroups.

Response: We agree that possibility of meta-analysis should be discussed. In the revision, we discussed what meta-analysis might be possible in the future and how to assess the heterogeneity in the revision (see page 7, lines 47).

Reviewer: 2

Reviewer Name: Mark McGlinchey

Institution and Country: Guy's and St Thomas' Hospital NHS Foundation Trust, King's College London, United Kingdom

Comments to the Author :

Thank you for the opportunity to review this protocol which addresses a very clinically relevant research question. I have provided comments regarding the review checklist as well as specific queries regarding the protocol.

1) Review Checklist : 2- Is the abstract accurate, balanced and complete?

The authors provide an overview of the justification of the systematic review, methods and data analysis in the abstract. The authors could provide more details regarding some aspects of the methodology e.g. dates of electronic searches, inclusion of randomised controlled trials (this is only mentioned later in the abstract when discussing the assessment of risk of bias), justification for only performing a qualitative synthesis. The authors could also provide more clarity regarding which statements are strengths and which statements are limitations in the “Strengths and Limitations of this study” section.

Response: Thank you for the suggestions. We have provided more details in the abstract regarding the methodology in the revised manuscript, such as database search dates, inclusion of randomized controlled trials (see page 1, line 27) and justification of data synthesis (see page 1, line 33). Also, we have separated the “Strengths and Limitations of this study” into “Strengths of this study” (see page 1, line 45) and “Limitations of this study” (see page 1, line 54).

2) Review Checklist : 13-Is the supplementary reporting complete (e.g. trial registration; funding details; CONSORT, STROBE or PRISMA checklist)?

The authors have referred to using the PRISMA-P checklist to guide their review protocol, which is an appropriate checklist. Could the authors complete PRISMA-P checklist and attach it as a supplementary file?

Response: We included a copy of the PRISMA-P checklist indicating the page/line numbers of this protocol in the supplementary table 1.

3) Review Checklist : 15-Is the standard of written English acceptable for publication?

The standard of written English is currently not acceptable for publication. For example:

- there are errors in subject-verb agreement
- o “previous evidence for effective treatments that recovers hand function...”

- o “to identify interventions that has potential to effectively...”
- o “currently this cohort of stroke survivors are largely ignored for hand function rehabilitation”
- there are omissions of the definite article when required and inclusions of the definite article when not required
- o “Generally, hemiparesis impacts the movement function of [the] hand and wrist more than [the] shoulder and elbow.”
- o “[The] Above features results in the abnormal involuntary coupling...”
- o “As we know, the hand movements play a core role in upper limb function...”
- o “The PT is defined as ‘services to individuals and populations to develop, maintain and restore maximum movement
- there are misspellings of commonly used words
- o “trials” is spelled as “trails” in the Types of Study, Participants and Analyses if Subgroups or Subsets sections
- o “trunk” is spelled as “truck” in the Discussion section

Response: We apologize for mistakes of written English. In the revised version, we have paid extra efforts on checking grammar and spelling.

- there are sentences where words are used that reduced the clarity of the sentence:
 - o “With the progress of rehabilitation science and tool development, results from small clinical trials have been available.” Do the authors mean that results from small clinical trial are now available thereby justifying the systematic review?
 - o “Secondary outcome measures will include kinematic analysis of hand movement, possible improvements of quality of life and possible mental health improvements related to the practice of interventions”. Do the authors mean that they will possibly include outcomes measures pertaining to quality of life and mental health?
 - o “To the best our knowledge, this is the first systematic review that attempts to sort out the hand rehabilitation approaches...” Do the authors mean that they will highlight certain hand rehabilitation approaches the many available hand rehabilitation approaches? Do the authors mean that they will divide the different hand rehabilitation approaches into different categories?

Response: We apologize for sentences where the words used reduced the clarity of the sentence. Those sentences with confusing words were rewritten to be clearer and more understandable (see page 1, line 17; page 5, line 57; page 8, line 46).

4) Specific Queries : Eligibility Criteria

Types of Studies

The authors have stated they will only include RCTs published in English, but they have not justified why they will only include RCTs and they have not justified why they will only include studies published in English. This latter aspect has the risk of excluding RCTs completed in countries where English is not the main language or where articles are written in another language. For example, a recent Cochrane review by Pollock et al. and published in 2014 (Physical rehabilitation approaches for the recovery of function and mobility following stroke) included 96 studies, over half of which were carried out in China. As there was a need to translate articles written in Chinese, this would suggest that there may be potentially eligible articles that may be excluded by the proposed search strategy.

Response: In this study, we will only include RCTs published in English mainly for the purpose of avoiding potential bias caused by language problems. English is generally perceived to be the universal language of science. Most of the high-quality clinical studies will have their results published in English. Such as for studies carried in China, according to Chinese scientific research policy, government funded clinical trials are encouraged to publish their results in English. Therefore, we add this language limitation to this review protocol. On the other hand, we do agree that this limitation may cause potential bias due to the exclusion of RCTs that do not publish in English. We have added discussion of such potential bias in the revision (see page 1, line 59).

5) Specific Queries : Eligibility Criteria

Participants

The authors have included scores on functional assessments to identify patients with moderate to severe unilateral arm and hand dysfunction (Fugl-Meyer UE scale, Chedoke-McMaster Stroke Assessment) but they have not referenced the scores to indicate that they can be used to identify eligible participants. The authors should include references to justify these scores as indicators of severity of hand dysfunction.

Response: Agree. In this study, stroke patients with Fugl-Meyer Upper Extremity Scale scores < 45 and Chedoke-McMaster Stroke Assessment score ≤ stage 4 are typically considered as moderate to severe subjects^{1 2}. We included these criteria (see page 5, line 25) and references in the revised manuscript (see page 14, line 23).

6) Specific Queries : Eligibility Criteria

Types of Interventions

The authors have stated that they will select all trials assessing a rehabilitation method- PT and OT. It is not usual to describe physical therapy/physiotherapy and occupational therapy as rehabilitation methods. They may be considered as interventions which in themselves encompass many different, individual interventions, such as exercise therapy, manual techniques, task-specific practice and education. Will the authors just include RCTs investigating the effects of “physiotherapy” or “occupational therapy” as a package of care, or will they include RCTs investigating the effect of individual interventions, such as CIMT or FES?

Response: Your suggestions are appreciated. We have revised corresponding sentences according to your suggestions, as “The interventions here encompass many different, individual interventions, such as FES, mirror therapy, robot training, CIMT, brain-computer interface, repetitive transcranial magnetic stimulation, etc. (see page 5, line 39)”

7) Specific Queries : Search Strategy for the identification of relevant studies

The authors have included an example of a search strategy to be used for the systematic review, which seems quite brief. Whilst this may be due to the design of the Cochrane Library Database, it does not include the main interventions that the authors have identified (physical therapy/physiotherapy and occupational therapy). Could the authors include a more detailed search strategy?

Response: As you recommended, we have added the main interventions (such as FES, mirror therapy, robot training, CIMT, brain-computer interface, etc.) that we identified into the search strategy in the revised manuscript (see page 6, line 36).

8) Specific Queries : Strategy for Data Synthesis

The authors have stated that they will provide a qualitative synthesis to summarise the main results. They state later that they anticipate that there will be limited scope for a meta-analysis due to the range of different outcome measures and heterogeneity of interventions across the existing trials based on initial screening. However, unless they have completed the data extraction process of the eligible studies (in which case it might be too late to publish the protocol), they cannot know for certain if they will not be able to do a meta-analysis, which is the more common method of presenting results from systematic reviews investigating the effectiveness of health care interventions. The authors should justify their strategy more clearly.

Response: Thanks for this comment. Indeed, at this stage, we don't know for certain if we will be able to do a meta-analysis. In the revision, we discussed the possibility for meta-analysis, and how to perform the assessment of heterogeneity (see page 7, line 41).

VERSION 2 – REVIEW

REVIEWER	Bichun Ouyang RUMC, USA
REVIEW RETURNED	28-Aug-2019

GENERAL COMMENTS	The authors have addressed my questions in this revision.
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REVIEWER	Mark McGlinchey King's College London, England
REVIEW RETURNED	01-Sep-2019

GENERAL COMMENTS	Thank you for the opportunity to review again this revised protocol which addresses a very clinically relevant research question. I have noted that the authors have responded to my previous comments. I would recommend publication of this systematic review protocol.
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