PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Tele-UPCAT: Study Protocol of a Randomized Controlled Trial of a Home-Based Tele-monitored UPperLimb Children Action observation Training for Participants with Unilateral Cerebral Palsy
AUTHORS	Sgandurra, Giuseppina; Cecchi, Francesca; Beani, Elena; Mannari, Irene; Maselli, Martina; Falotico, Francesco; Inguaggiato, Emanuela; Perazza, Silvia; Sicola, Elisa; Feys, Hilde; Klingels, Katrijn; Ferrari, Adriano; Dario, Paolo; Boyd, Roslyn; Cioni, Giovanni

VERSION 1 – REVIEW

REVIEWER	Hsiu-Ching Chiu I-Shou University, Taiwan
REVIEW RETURNED	20-Jun-2017

GENERAL COMMENTS	The novelty of topic under investigation is about the environment of intervention. The effectiveness of Upper limb children action observation training has been proved by themselves in their previous paper. However, there is no section about how authors adjust this approach to home, such as instructions of parents or trainers and recording process of intervention. For example, authors should provide acceptability form for both participants and parents as well as safety form during intervention because the intervention environment has been changed to home. The other problem is age range of participants is too wide. Some English problems, such as “subjects” should be “participants” (there are more, but I just gave one example). Research questions are too descriptive, so it is not easy to understand. All of these above problems make this manuscript like a thesis only. Since there are so many omissions, the significance under investigation is questionable.

REVIEWER	Margaret Wallen Australian Catholic University Australia
REVIEW RETURNED	23-Jun-2017

GENERAL COMMENTS	This is an exciting project with a valuable aim of making an upper limb intervention more accessible to children and youth with UCP. The paper is well written and a pleasure to read. The investigators are well known and highly respected. I believe the following requires addressing prior to publication. The required revisions will enhance the clarity and depth of reporting of this important and clearly sound study. I look forward to reading the results and understanding its application to clinical practice and

	outcomes for children, youth and young adults with unilateral CP. Please use the word “participant” in lieu of all instances of “subjects” in title and throughout. Also instead of carrying out assessments/interventions “on” participants, consider: “completed with participants” or “Participants completed” Please reference your work which is mentioned in the final sentence of para 2. Please state the order of baseline assessment and randomisation in the text Describe standard care, what are participants likely to be involved in, how is the intensity of this standard care to be captured. Is the diary of daily activities intended to capture a description of other intervention that was completed by both study arms during the study period? Was there any consultation with families and particularly adolescents and young adults about the feasibility and acceptability of the study and/or intervention? If so, please report this. T2 (8 weeks) is defined early in the methods but T3 is not defined at its first mention and T4 is mentioned on page 5 in two places and not mentioned again Both SPIRIT and CONSORT statements are upper case “but will still obtain their relative clinical assessments”. This statement is unclear. Will they continue to be assessed or will the existing assessment data still be used or will the assessment information be reported back to families? I am not clear about the House Functional Classification System inclusion criteria. It states that children are included if they have mild to moderate impairment, but they also have minimal ability to grasp/hold. The latter is not consistent with mild and moderate impairment. It also specifies that the HFCS score for inclusion is ≥2, which includes ability from significant impairment through to almost no impairment. Please make this inclusion criteria clear The inclusion criteria around having sufficient cooperation, cognition and communication to participate in intervention activities” – requires more information about what ability this requires and how it would be determined by those undertaking the recruitment. Before the material on AOT library, the intervention needs to be described to give an overview before defining the specific features. For instance intervention is 2 sessions per day (21 days?) of 60 mins per session during which participant watches a model completing xxx activities and then imitates them etc. Include total dose expected. Also please specify if child observes a mirror or inverted image of the way they are going to complete the activity. I would like more information about the set up and training. Who takes the equipment to the house, how long does it take to set up, how much education is given to participant and family to use the ICT during the study period. What support is available during the intervention? ICT is apparently customised, but it sounds like only the set up is customised according to House level? How is it customised? Not only is this information important to know in terms of fully reporting the intervention, but is essential for understanding how the results might ultimately apply to the stated objective of increasing accessibility of this type of intervention to “a large number of children and young people with UCP (e.g. subjects that live far

	from the clinical centres)". Refer to TIDieR guidelines and Sakzewski (2016) Do we really know what they were testing? Incomplete reporting of interventions in randomised trials of upper limb therapies in unilateral cerebral palsy. Research in Developmental Disabilities. The sentence: "When possible, videos are inverted…" is not clear. Is it so that all participants will watch the same video but the image may be inverted so that they watch a mirror (or otherwise) image of their own performance. Table 1 – Please indicate which tasks are demonstrated as unimanual and which as bimanual activities The sentence around Line 30 starting: A dedicated software, appears unfinished. p9 Please justify wide age group – it seems a heterogenous group given evidence of neuroplasticity, possibility of age related differences in responses, feasibility to complete with youth and young adults (especially to have a parent supervisor) "couple of Actigraphs (wGT3X-BT, wActiSleep-BT) worn on both wrists – I read this as 2 actigraphs worn on both wrists ie 4 actigraphs, is this correct? It is not clear in the aims where the ABIHAND-Kids and BBT fit in. The measures are introduced in a sequential manner, for instance these two measures are not mentioned in the aims, BBT is first mentioned on page 6 but ABILHAND-Kids not until page 10. There are several assessments which are not validated across the entire age range. Please include the validated age range for each assessment and the reasons used for the ages for which the measures are not validated, for instance perhaps that they are being used in this age group in the absence of an alternative measure and to enable an assessment to be collected across all participants regardless of age. Although readers are directed to the AHA website, the description of the AHA as it relates to this study should be specified, for example, that Kids-AHA V5 is used for children 5 to 12 years and that Ad-AHA (and what this stands for) for the older age group. The reader should understand the age group to which the Ad-AHA applies, what Ad-AHA stands for, a specific reference for it and what tasks will be used, for instance that it involves a board game (or sandwich making task) BBT. It is not clear that the box, not the blocks, has a partition in the middle. Also it is important to clarify that the test involves the number of blocks transported in 1 minute. ABILHAND-Kids. Please specify the age range for which is it validated. Please comment on how the scores form ABILHAND and ABILHAND-Kids can be used on a common metric across the tests for analysis for the participant group as a whole. Outcome measure vi. The description is unclear, what is done? Also the references relate to infants. What is the justification or plan for use in this older group? Is it exploratory? The timing of actigraph wear is not clear. i.e. "between T0 and T1 or T1 and T1 plus and between T0 and T1 or after T1 or T1 plus". Does the AOT group wears it during 3 week intervention as well as for three weeks after? Does the standard care group wear it during standard care and then during AOT 3 week period?

	The methods/outcome measures sections doesn't address how aim iv) will be addressed: "report that ICT rehabilitation in a home setting is as comfortable, reliable, feasible and effective for UCP subjects and their families as rehabilitation in a clinical centre" p5. Please include how this very important information will be ascertained. The cost effectiveness analysis mentioned in the outcome measures needs to be introduced in the aims section. The following needs to be referenced: "Health care utilisation will be collected using a resource use questionnaire previously used in CP studies" Please report who supports the families to complete all the questionnaires and where the assessments are completed? At some point in this protocol the nature of the data used for each outcome measure for analysis needs to be presented, ie which data from each measure will be analysed, type of scores generated from each test (e.g., logits), range of possible scores, direction of score. This should include whether total scores and all domain scores will be analysed. Until the statistical analyses section, there is no mention that this is an exploratory study. Then this is the reason given for avoiding a Bonferroni correction for multiple comparisons. And, in a study which appears to have had a sample size calculation, what is the rationale for considering this to be exploratory and not requiring Bonferroni correction? There is a significant number of analyses at each time point – depending on whether domains of each test are included as well as total scores. Figure 1 flowchart doesn't mention the economic evaluation. It reports that T3 is at 16 weeks, whereas the text specifies 24 weeks. It states the intervention is AOT training and then introduces "UL physical training" which is not addressed in the text. The actigraph is measured at each of the time points. There is insufficient explanation of what is measured at each time point. Do participants wear the actigraph for a 3 week period prior to the assessment or for the duration of the assessment only – this requires clarification.

VERSION 1 – AUTHOR RESPONSE

Editorial Requirements of 03/08/2017:
1. You have cited Figure 3 right after Figure 4 which makes your Figure citations incorrect. Please review again your main document and ensure that all Figure citations will be cited and will appear ascending order.
(R) We have inverted Figure 3 with Figure 4 so that they will appear in ascending order.
Editorial Requirements of 01/08/2017:
1. Please ensure that the Funding statement in your main document and Scholar One submission system are the same.
(R) We have copied the statement from the main document to the Scholar One; they are now identical.
2. Please review again your main document and ensure that all references will be cited and will appear in ascending numerical order.
(R) We have checked the references according to the request.
3. Please provide another copies of your figures with better qualities. NOTE: They can be in TIFF or JPG format and make sure that they have a resolution of at least 300 dpi. Figures in PDF, DOCUMENT, EXCEL and POWER POINT format are not acceptable.
(R) We have improved the quality of our figures reaching a resolution of 300 dpi

4. Please combined Figure 3a and 3b on one figure file.
(R) We have combined the two figures in one.
Editorial Requirements 03/07/2017:
1 - Please complete and include a SPIRIT check-list, ensuring that all points are included and state the page numbers where each item can be found: the check-list can be downloaded from here: http://www.spirit-statement.org/
(R) We have filled in the SPIRIT Statement
2 - Please revise the Strengths and Limitations section (after the abstract) to focus on the methodological strengths and limitations of your study.
(R) We have revised the Strengths and Limitations section focusing of the methodology of our study
Reviewer(s)' Comments to Author:
Reviewer: 1
Reviewer Name: Hsiu-Ching Chiu
Institution and Country: I-Shou University, Taiwan
1 - The novelty of topic under investigation is about the environment of intervention. The effectiveness of Upper limb children action observation training has been proved by themselves in their previous paper. However, there is no section about how authors adjust this approach to home, such as instructions of parents or trainers and recording process of intervention.
(R) We have added details about the process of intervention at home, mainly in the Experimental Training subsection of the Methods/Design (page 8)
2. For example, authors should provide acceptability form for both participants and parents as well as safety form during intervention because the intervention environment has been changed to home.
(R) We have added the acceptability assessment in the study design and in the outcome measures.
3. The other problem is age range of participants is too wide.
(R) We agree with this issue, suggested also by the Reviewer 2 in her point 17, but, from our point of view, a wide age range of participants is also a point of strength. We aim to provide the AOT to a large group of patients with UCP and the possibility of customization of the technology offers to us the opportunity to deliver the AOT respecting the age differences. In order to overcome the problem for the RCT we have planned an age stratification. Moreover, in the statistical analysis, we have planned further analyses considering age and other factors as variables.
4. Some English problems, such as “subjects” should be “participants” (there are more, but I just gave one example).
(R) We have replaced “subjects” with “participants” and we have revised the text
5. Research questions are too descriptive, so it is not easy to understand. All of these above problems make this manuscript like a thesis only. Since there are so many omissions, the significance under investigation is questionable.
(R) Following Reviewer’s suggestions, we have revised the whole MS, including also aims and hypotheses.
Reviewer: 2
Reviewer Name: Margaret Wallen
Institution and Country: Australian Catholic University, Australia
1. This is an exciting project with a valuable aim of making an upper limb intervention more accessible to children and youth with UCP. The paper is well written and a pleasure to read. The investigators are well known and highly respected. I believe the following requires addressing prior to publication. The required revisions will enhance the clarity and depth of reporting of this important and clearly sound study. I look forward to reading the results and understanding its application to clinical practice and outcomes for children, youth and young adults with unilateral CP.
(R) We would like the reviewer for her interest and the useful suggestions we hope to have completely satisfied, improving our study protocol
2- Please use the word “participant” in lieu of all instances of “subjects” in title and throughout. Also instead of carrying out assessments/interventions “on” participants, consider: “completed with participants” or “Participants completed”

(R) According to the requests of both Reviewers we have changed the MS (see previous reply to reviewer 1, point 2).
3- Please reference your work which is mentioned in the final sentence of para 2.
(R) We have added the reference.
4- Please state the order of baseline assessment and randomisation in the text
(R) We have added it in the study design section.
5- Describe standard care, what are participants likely to be involved in, how is the intensity of this standard care to be captured. - Is the diary of daily activities intended to capture a description of other intervention that was completed by both study arms during the study period?
(R) Yes, the diary was intended to record the other interventions in both groups. We have specified what is referred as standard care in the relative section (page 8) and how it is recorded with the diary in the study design (page 4)
6- Was there any consultation with families and particularly adolescents and young adults about the feasibility and acceptability of the study and/or intervention? If so, please report this.
(R) No specific consultation had been done neither with families or with children. However for the software design a specific literature analysis have been carried out to study which features (in term of images and of stories) are mainly attractive for the different ages (as added in the subsection Tele-UPCAT system on page 6). Another important point is that the need of delivering the AOT at home raised by the participants (children and their caregivers) enrolled in the previous clinical study (Sgandurra et al, 2013); they were greatly satisfied by the experience but complained of the need to come for three weeks, each working day, at the clinical center (as stated at the end of Background on page 3).
7- T2 (8 weeks) is defined early in the methods but T3 is not defined at its first mention and T4 is mentioned on page 5 in two places and not mentioned again
(R) We have changed the MS accordingly
8- Both SPIRIT and CONSORT statements are upper case “but will still obtain their relative clinical assessments”. This statement is unclear. Will they continue to be assessed or will the existing assessment data still be used or will the assessment information be reported back to families?
(R) We agree that the sentence was not clear and we have modified the text (page 5).
9- I am not clear about the House Functional Classification System inclusion criteria. It states that children are included if they have mild to moderate impairment, but they also have minimal ability to grasp/hold. The latter is not consistent with mild and moderate impairment. It also specifies that the HFCS score for inclusion is ≥2, which includes ability from significant impairment through to almost no impairment.
Please make this inclusion criteria clear
(R) We agree that it was not clear and we have revised the criteria and changed the text accordingly.
10- The inclusion criteria around having sufficient cooperation, cognition and communication to participate in intervention activities” – requires more information about what ability this requires and how it would be determined by those undertaking the recruitment.
(R) We have specified the cognitive level and how and when it is evaluated.
11- Before the material on AOT library, the intervention needs to be described to give an overview before defining the specific features. For instance intervention is 2 sessions per day (21 days?) of 60 mins per session during which participant watches a model completing xxx activities and then imitates them etc. Include total dose expected. Also please specify if child observes a mirror or inverted image of the way they are going to complete the activity.
(R) We have specified better the above points, adding an introductive session at the beginning of study treatment
12- I would like more information about the set up and training. Who takes the equipment to the house, how long does it take to set up, how much education is given to participant and family to use the ICT during the study period.
(R) We have added these information in the section Experimental training of the MS (page 8)

13. What support is available during the intervention? ICT is apparently customised, but it sounds like only the set up is customised according to House level? How is it customised? Not only is this information important to know in terms of fully reporting the intervention, but is essential for understanding how the results might ultimately apply to the stated objective of increasing accessibility of this type of intervention to “a large number of children and young people with UCP (e.g. subjects that live far from the clinical centres)”.
Refer to TIDieR guidelines and Sakzewski (2016) Do we really know what they were testing? Incomplete reporting of interventions in randomised trials of upper limb therapies in unilateral cerebral palsy. Research in Developmental Disabilities.
(R) The ICT in terms of hardware (desk, webcam, actigraphs, sensors) are identical for the whole sample while the software (video, storyboard) are customized to age and HFCS level. Moreover, we have filled in the TIDieR guidelines (provided as attached file) and modified the text accordingly
14- The sentence: “When possible, videos are inverted…”is not clear. Is it so that all participants will watch the same video but the image may be inverted so that they watch a mirror (or otherwise) image of their own performance.
(R) We agree that the sentence was not clear and we have changed it accordingly.
15- Table 1 – Please indicate which tasks are demonstrated as unimanual and which as bimanual activities
We have specified the unimanual and bimanual activities in the table, as suggested .
16- The sentence around Line 30 starting: A dedicated software, appears unfinished. p9
(R) We have revised the sentence.
17- Please justify wide age group – it seems a heterogenous group given evidence of neuroplasticity, possibility of age related differences in responses, feasibility to complete with youth and young adults (especially to have a parent supervisor)
(R) As replied to review 1 at point 3, the wide age group was chosen in order to explore potential age related differences in the usability and effectiveness of Tele-UPCAT platform. For the correction of possible bias an age-matched randomization has been planned. The system is managed by the parents of children but it could be directly managed by teenagers and young participants who prefer do not have a supervision. All these factors will be registered and evaluated for the data analysis (as added in the statistical analysis section).
18- “couple of Actigraphs (wGT3X-BT, wActiSleep-BT) worn on both wrists – I read this as 2 actigraphs worn on both wrists ie 4 actigraphs, is this correct?
(R) Two actigraphs were worn, one for each wrist. We e have changed the text accordingly.
19- It is not clear in the aims where the ABIHAND-Kids and BBT fit in. The measures are introduced in a sequential manner, for instance these two measures are not mentioned in the aims, BBT is first mentioned on page 6 but ABILHAND-Kids not until page 10.
(R) It was a mistake and, as suggested, we have introduced ABILHAND-Kids and BBT also in the aims.
20- There are several assessments which are not validated across the entire age range. Please include the validated age range for each assessment and the reasons used for the ages for which the measures are not validated, for instance perhaps that they are being used in this age group in the absence of an alternative measure and to enable an assessment to be collected across all participants regardless of age.
(R) We have included the age range for which the planned outcome measures are validated and, as suggested, we have explained the reasons for using them for older ages.
21- Although readers are directed to the AHA website, the description of the AHA as it relates to this study should be specified, for example, that Kids-AHA V5 is used for children 5 to 12 years and that Ad-AHA (and what this stands for) for the older age group. The reader should understand the age group to which the Ad-AHA applies, what Ad-AHA stands for, a specific reference for it and what tasks will be used, for instance that it involves a board game (or sandwich making task)
(R) We have changed the MS accordingly to the reviewer’s suggestions.

22- BBT. It is not clear that the box, not the blocks, has a partition in the middle. Also it is important to clarify that the test involves the number of blocks transported in 1 minute.
(R) We have changed the MS accordingly to the reviewer's suggestions
23- ABILHAND-Kids. Please specify the age range for which is it validated. Please comment on how the scores form ABILHAND and ABILHAND-Kids can be used on a common metric across the tests for analysis for the participant group as a whole.
(R) In relation to reviewer's suggestion on how to manage the two different forms of ABILHAND, also revising deeply the literature on which form is commonly used for adolescents and young people with UCP, we have decided to skip the ABILHAND and use only the ABILHAND-Kids to have a unique measure.
24- Outcome measure vi. The description is unclear, what is done? Also the references relate to infants. What is the justification or plan for use in this older group? Is it exploratory?
(R) Taking account our previous experience in developing sensorized toys for infants, we have designed a new sensorized object composed by two load-cells and an embedded switch for the measurement of the grasping time and maximum grasping force of the affected hand and the delay time between unaffected and affected hand in reaching for the object. We have clarified this issue also in the text.

25- The timing of actigraph wear is not clear. i.e. "between T0 and T1 or T1 and T1 plus and between T0 and T1 or after T1 or T1 plus". Does theAOT group wears it during 3 week intervention as well as for three weeks after? Does the standard care group wear it during standard care and then during AOT 3 week period?
(R) We agree with the reviewer that the timing of actigraph wearing was not clear and we have changed the text accordingly.
26- The methods/outcome measures sections doesn't address how aim iv) will be addressed: "report that ICT rehabilitation in a home setting is as comfortable, reliable, feasible and effective for UCP subjects and their families as rehabilitation in a clinical centre" p5. Please include how this very important information will be as certained.
(R) As replied to Reviewer 1 in the point 2, we have added the acceptability assessment in the study design and in the outcome measures (point ix on page 11).
27- The cost effectiveness analysis mentioned in the outcome measures needs to be introduced in the aims section. The following needs to be referenced: "Health care utilisation will be collected using a resource use questionnaire previously used in CP studies"
(R) We have added the cost-effectiveness analysis as aim and added the missed reference according to the reviewer's suggestions.
28- Please report who supports the families to complete all the questionnaires and where the assessments are completed?
(R) Questionnaires will be completed by parents and/or participants at home and if doubts will occur, child neurologists or therapists will be available to discuss items not clear to them. This sentence was added at the beginning of outcome measures section.
29- At some point in this protocol the nature of the data used for each outcome measure for analysis needs to be presented, ie which data from each measure will be analysed, type of scores generated from each test (e.g., logits), range of possible scores, direction of score. This should include whether total scores and all domain scores will be analysed.
(R) We have added in the description of each outcome measure the required data.
30- Until the statistical analyses section, there is no mention that this is an exploratory study. Then this is the reason given for avoiding a Bonferroni correction for multiple comparisons. And, in a study which appears to have had a sample size calculation, what is the rationale for considering this to be exploratory and not requiring Bonferroni correction? There is a significant number of analyses at each time point –depending on whether domains of each test are included as well as total scores.
(R) We think that it is upstanding calculate the projected treatment effect on the previous AOT study but the different delivering of the AOT account for the exploratory character of the present study. We

have declared the exploratory nature at the beginning of the MS (study design and sample size sections).
31- Figure 1 flowchart doesn't mention the economic evaluation. It reports that T3 is at 16 weeks, whereas the text specifies 24 weeks.
(R) 24 weeks, written in the text, referred to weeks after the end of AOT training while 16 weeks, written in the figure, referred to weeks after T2. For more clarity, we have indicated also in the figure 24 weeks. We have also added the economic analysis.
32- It states the intervention is AOT training and then introduces "UL physical training" which is not addressed in the text.
(R) We have removed this definition
33- The actigraph is measured at each of the time points. There is insufficient explanation of what is measured at each time point. Do participants wear the actigraph for a 3 week period prior to the assessment or for the duration of the assessment only – this requires clarification.
(R) The participants wear the actigraphs both during the assessment and during the 3 week periods. We have better explained it in the text and changed the Figure 1.

VERSION 2 – REVIEW

REVIEWER	Margaret Wallen Australian Catholic University Australia
REVIEW RETURNED	24-Aug-2017

GENERAL COMMENTS	The authors have carefully attended to the suggested amendments and this paper now provides a more comprehensive description of the intervention and clarified several additional points. Some of the amendments have resulted in a couple of areas which are somewhat unclear. I believe that addressing the following would finalise this paper leading to a well written, well described protocol. The 1st and 2nd paragraphs would benefit by a linking sentence to i) give context to the UPCAT study II) make clear what the limits refer to in the second paragraph and iii) give "this approach" referred to in first line of second paragraph a subject. The linking sentence could mention what children are required to do and that it is lab based. Line 31 of background "youngs". Is this meant to be young children or young people? A context is required for the early intervention in preterm infants towards the end of the second paragraph of the background to make its inclusion relevant - what was the intervention. This paragraph also goes on to mention a framework. I am not sure that a framework has been mentioned, an intervention and approach are the concepts introduced in the previous sentences. The term "quantitative measurement of manual ability" presented in the last paragraph of the background is not clear until well into the methods. Some of the previous measures listed in this paragraph may also be viewed as quantitative. I suggest adding clarification - quantitative measurement of manual ability obtained using sensitised objects and TeleCAT. It appears from this paragraph that the TeleCAT measures quantitative measurement of manual ability. The methods, however in the description of the quantitative measurement of manual ability, doesn't mention TeleCAT. It would be useful to clarify this. It would be useful to finish the background section with stating the aims of the study. They are integrated into the methods, but are more conventionally placed at the end of the introductory section. There is now more clarity about the parent feedback about

	feasibility. However the study design section focuses on a questionnaire to grade 'feelings' about proposed activities. Perhaps it might be more accurate to say the questionnaire is ascertaining parents' perception about the experiences of using Tele-CAT. In addition the methods section says the questionnaire is completed using semistructured interview which seems at odds with the multiple choice options advised in this part of the paper. Can this be made clearer and consistent? Next paragraph – CONSORT in upper case The final sentence of the Blinding section isn't clear – I can't work it out in order to provide a suggestion. If there are assessment conducted outside of the study, why would they be mentioned? Is it being suggested that assessments completed after participant withdrawal will be included in the research. Or does it mean that children can withdraw from the intervention phase but invited to continue to be involved in the ongoing study assessments? The inclusion criteria related to the HFCS remains confusing. What about considering something like: House Functional Classification System score ≥2, that is, able to passively hold an object in the hand or better. The second sentence under "Study Treatment" heading is not clear and needs to be amended. Thank you for amending the information about inverting the images on the video. However, I am still not clear. The current description suggests that children with right UCP view an actor using their own right hand for unilateral actions, therefore they are NOT viewing a mirror image but viewing a reversed image. If this is the case, then the second last sentence is clear. The last sentence is not clear, and could read something like: For children with left UCP the same images are reversed. Information about the assessments is now more comprehensive and inclusion of justifications for usage outside validated age groups is responsible. The description of the CPQOL needs to be clearer – including using correct terms. For instance it appears, but important to confirm, that the primary caregiver version was used for younger children and the teen self report version was used by older children. The description of the quantitative measurement during unimanual and bimanual manipulation in the outcome measures section doesn't make it clear that it is part of the TeleCAT technology or how it is part of TeleCAT. Statistical analysis section. "To test our first hypothesis, an intention to treat analysis will be carried out, evaluating between-group differences for primary and secondary outcome measures at the primary endpoint (T1), compared with T0, by means of parametric or non-parametric tests for unrelated samples." Please add in the words change scores in this sentence to reinforce that the difference from baseline between groups is being analysed. If change scores are not being used, then I believe the words "compared with T0" need to be deleted. The next sentence needs more information about the purpose of the "exploratory analysis", what is this and how does it relate to study aims. Figure 2 – schedule of enrolment etc. There are 3 horizontal arrows. I think perhaps these are not in the correct places. Figure 3 is a very elegant infographic which contains useful information. I believe there is too much detail to be included in either a print journal or an electronic supplementary file. Strengths and limitations. A new issue has been raised about measurement of visual attention. I don't believe it is appropriate to raise this issue without it being addressed in the body of the protocol

	I appreciate the amendment of the term “subjects” to participants – there are still instances of “subjects” and “patients” to be replaced. Again, I look forward to seeing this really interesting protocol published and the results of the study being made available.

REVIEWER	Hsiu-Ching Chiu Department of Physical Therapy, School of Medicine for International Students, I-Shou University, Taiwan
REVIEW RETURNED	31-Aug-2017

GENERAL COMMENTS	Comments General comments Previous problems still exist. Authors need to clarify whether this is feasibility study or randomised controlled trial. If authors haven’t confirmed this is feasible, this could be feasibility study before they run a trial. However, there is no section about how authors adjust this approach to home, such as instructions of parents or trainers and recording process of intervention. For example, authors should provide acceptability form for both participants and parents as well as safety form during intervention because the intervention environment has been changed to home. The other problem is age range of participants is too wide. Some English problems, such as “youngs” should be “younger population” or “children” in the introduction (there are more, but I just gave one example). Furthermore, there are too many repetitive section, such as design. Research questions are too descriptive, so it is not easy to understand. All of these above problems make this manuscript like a thesis only. Since there are so many omissions, the significance under investigation is questionable. Some examples to tidy up paragraph (there are more, so the whole paper will be required to be re-written): *Research questions: 1. Is it feasible for children with cerebral palsy to train XXX (this is also the part where I cannot see why authors use this intervention) at home using *ICT* platform? 2. Can 3 weeks of *ICT* training improve XXX and does this carry over to improvements in long term? 3. …a cost-effective….? *Design- why repeat design twice?

	*Study treatment (this should be “intervention) Experiemental group will undertake XXX at home using XXX for XX minutes a session, XX times a week over 3 weeks, ie, XX sessions. XXX games will be chosen that target XXX. Each session consisted of playing ….. Control group received… Both received… Each participant in experienmental group will be assigned one of XX therapists trained in the XX who supervised one session a week and parents supervise the other XX sessions….. *Outcome measures *Feasiblity* Safety… Parents’ report… Participants’ report…

REVIEWER	Anthony Terrence O'Brien Independent Colombia
REVIEW RETURNED	11-Sep-2017

GENERAL COMMENTS	Manuscript bmjopen-2017-017819 is a protocol for an exploratory, cross-over design (waitlist), randomized clinical trial investigating the application of Action Observation Training (AOT) delivered via a new Information and Communication Technology (ICT) platform, Tele-UPCAT, in a home setting with children and young people with Unilateral Cerebral Palsy (UCP). The main outcome is Assisting Hand Assessment, while secondary and other outcomes are: The Melbourne Assessment 2, Box and Block test, ABILHAND, Participation and Environment Measure-Children and Youth (PEM-CY) and Cerebral Palsy Quality of Life Questionnaire (CP-QoL), and quantitative reaching and grasphing measurements from a sensorized object, in upper limb activities and daily life activities detected from 2 independent wrist-worn devices (Actigraphs GXT3+). The clinicaltrial.gov registration number is NCT03094455 and the PICOT match the clinicaltrials.gov description set forth within this manuscript/protocol. This trial started on March 29, 2017 and is also the continuation of the groups prior work 1) Upper limb children

	action-observation training (UP-CAT): a randomized controlled trial in Hemiplegic Cerebral Palsy, 2) Randomized trial of observation and execution of upper extremity actions versus action alone in children with unilateral cerebral palsy. The version received is a revised manuscript (already peer-reviewed), and the authors have made a very comprehensive and clear response towards the prior peer-review comments. Some minor aspects that they may consider are: 1) Page 6, lines 7-12: To account for the large age difference the groups will be dichotomized and also categorized according to their HFCS. The sample size is derived from the group's 2 prior works, and the sample size in those projects are from Elliason et al (Effects of constraint-induced movement therapy in young children with hemiplegic cerebral palsy: an adapted model.). The concern is that due to the clustering of groups, if the sample size is adequately powered to find a significant difference for the subgroups designed within this manuscript. If it is, the authors may consider stating that it was accounted for. 2) Page 7, line 29: "[…] left UCP the previous videos where tipped over if they maintained the same characteristic of the […]" Rather than tipped over, authors may consider writing that the image was horizontally flipped. 3) Page 9, line 49. Remove the word "will" 4) Page 11-12, though ITT is the planed statistical analysis, do authors have a plan for measuring adherence or taking into account any deviations from adherence? This though not described in the clinicaltrials registry, and is of important when testing home based devices (well almost any intervention but more so for a trial like this). If "The age, HFCS level, characteristics of usual care (in both groups), supervision of caregiver will be analysed for further exploratory analyses" alludes to such, it could be reworded as is not clear. Also if adherence it so be measured, authors may consider describing it in the outcomes and what implications it may have on the results, and the statistical analysis. Aside, if it is also possible to include the expected clinically significant difference in the primary outcome, it would be useful for interpreting changes. Finally, as this is a relatively small trial, though the objective is to look at grouped differences, the size permits for an individual/participant based analysis, and may be worth it. A paragraph on any descriptive analysis can also be included. 5) As there is a group which will be crossed-over, is there a wash out period or any intention to account for possible carry-over effect? 6) Any foreseeable limitations can also be described within the protocol 7) Authors can make reference in text to supplementary material (already provided) which describes devices etc (eg. Actigraphs GXT3+) Overall the authors touch on the important points for carrying out a home-based device based clinical trial, i.e.: 1) ensure that there is a means of training the person in charge of administering the intervention, 2) remote monitoring of compliance by a proxy (though not in real time, it is being monitored), 3) sufficient operating procedure resources are made available to participants and families, 4) easy to use devices, 5) fixed dosing/training parameters, and 6) safety monitoring. For future trials if it is possible to have on-going/live monitoring of compliance and a protocol for discontinuation, this will benefit the trials also. Otherwise it is a

	thoroughly planned protocol by a group with experience in this area. Thank you for the opportunity to review your work and best wishes in its successful completion and future contribution. Respectfully. Peer-reviewer BMJ-Open

REVIEWER	Dr Laura Bonnett University of Liverpool, United Kingdom
REVIEW RETURNED	18-Sep-2017

GENERAL COMMENTS	Although I did not review the original submission, I have been pleased to review this revised version of a protocol for an RCT of home-based Tele-UPCAT for participants with unilateral cerebral palsy. The protocol is generally very good. Although the proposed methodology is brief, this is acceptable for a protocol. The study design concerns me slightly. However, I do appreciate that it has been approved by the ethics committee. The design as it currently stands does not enable comparison of the long-term impact of Tele-UPCAT. However, it is acceptable to assess short term outcomes by comparing the results of the control and intervention groups at 3 weeks. For this reason I will accept the design as it stands within this protocol.

VERSION 2 – AUTHOR RESPONSE

Editorial Requirements:

- Please include an English model consent form as per the requirements of the SPIRIT checklist.

(R) We have provided the translation of Supplement material 2 (in Italian language) in English with the consent forms, adding Supplement material 3.

Reviewer(s)' Comments to Author:

Reviewer: 1

Reviewer Name: Hsiu-Ching Chiu
Institution and Country: Department of Physical Therapy, School of Medicine for International Students, I-Shou University, Taiwan
state any competing interests: None

1. Previous problems still exist. Authors need to clarify whether this is feasibility study or randomised controlled trial. If authors haven't confirmed this is feasible, this could be feasibility study before they run a trial.

(R) We aim to run a pilot (indicated as exploratory) RCT study that according to literature [e.g. Feeley et al., et al (2009). The importance of piloting an RCT intervention. Canadian Journal of Nursing Research, 41(2), 84–99] is the best option to test the feasibility of the features of a RCT, and as such requires random assignment of participants to a group. This type of studies allows us to assess both the feasibility and acceptability of the intervention and its design and procedures.

2. However, there is no section about how authors adjust this approach to home, such as instructions of parents or trainers and recording process of intervention. For example, authors should provide acceptability form for both participants and parents as well as safety form during intervention because the intervention environment has been changed to home.

(R) As already replied to the Reviewer in the previous submission, we have added details about the process of intervention at home, mainly in the Experimental Training subsection of the Methods/Design (page 8 and 9)

3. The other problem is age range of participants is too wide.
(R) We defend our inclusion criteria for age as groups will be matched for age/gender and then randomised so there will be equal allocation. We also believe that as the AOT training is very suitable for a large group of patients with UCP and the possibility of customization of the technology enables the opportunity to deliver the AOT irrespective of age differences. In the statistical analysis, we will account for the stratification by age bands and gender and have planned secondary analyses considering age and other factors as co-variables.

4. Some English problems, such as “youngs” should be “younger population” or “children” in the introduction (there are more, but I just gave one example).

(R) Following reviewer’s suggestion with have replaced “youngs” with “younger population” in the introduction (page 3) while the entire MS has been further revised by a tongue English native speaker (see acknowledgements on page 13), as already done in the previous submission.

5. Furthermore, there are too many repetitive section, such as design.

(R) The short section of methods/design has been revised to overcome these issues and to the list all aims and hypotheses. We conclude that all repetition has now been addressed.

6. Research questions are too descriptive, so it is not easy to understand.

(R) In the last revision we have removed the research questions, so it is not clear to us to which detailed research questions the reviewer is referring.

7. All of these above problems make this manuscript like a thesis only. Since there are so many omissions, the significance under investigation is questionable. Some examples to tidy up paragraph (there are more, so the whole paper will be required to be re- written):
*Research questions:
1. Is it feasible for children with cerebral palsy to train XXX (this is also the part where I cannot see why authors use this intervention) at home using ICT platform?
2. Can 3 weeks of ICT training improve XXX and does this carry over to improvements in long term?
3. …a cost-effective….?
*Design- why repeat design twice?
*Study treatment (this should be “intervention)
Experimental group will undertake XXX at home using XXX for XX minutes a session, XX times a week over 3 weeks, ie, XX sessions. XXX games will be chosen that target XXX. Each session consisted of playing …..
Control group received…
Both received…
Each participant in experimental group will be assigned one of XX therapists trained in the XX who supervised one session a week and parents supervise the other XX sessions…..

*Outcome measures
Feasiblity
Safety…
Parents' report…
Participants' report…

(R) We have made considerable modification to our manuscript, thanks also to the many suggestions for changes that we received to the first and second submission. We believe the paper has been considerably strengthened. Our opinion seems to be shared by the other 3 referees.

Reviewer: 2
Reviewer Name: Margaret Wallen
Institution and Country: Australian Catholic University, Australia
Please state any competing interests: Non declared

1. The authors have carefully attended to the suggested amendments and this paper now provides a more comprehensive description of the intervention and clarified several additional points. Some of the amendments have resulted in a couple of areas which are somewhat unclear. I believe that addressing the following would finalise this paper leading to a well written, well described protocol. The 1st and 2nd paragraphs would benefit by a linking sentence to i) give context to the UPCAT study II) make clear what the limits refer to in the second paragraph and iii) give "this approach" referred to in first line of second paragraph a subject. The linking sentence could mention what children are required to do and that it is lab based.

(R) We agree that the two paragraphs need to be better linked and we have changed the MS accordingly on page 3

2. Line 31 of background "youngs". Is this meant to be young children or young people?

(R) As suggested by the Reviewer #1 we have changed "youngs" with "younger population" (page 3)

3. A context is required for the early intervention in preterm infants towards the end of the second paragraph of the background to make its inclusion relevant - what was the intervention. This paragraph also goes on to mention a framework. I am not sure that a framework has been mentioned, an intervention and approach are the concepts introduced in the previous sentences.

(R) The intervention referred to on page 3 and, the framework mentioned has been changed as "field" (referred to ICT technologies for rehabilitation) and we have now incorporated this into the manuscript on page 3.

4. The term "quantitative measurement of manual ability" presented in the last paragraph of the background is not clear until well into the methods. Some of the previous measures listed in this paragraph may also be viewed as quantitative. I suggest adding clarification - quantitative measurement of manual ability obtained using sensitised objects and TeleCAT. It appears from this paragraph that the TeleCAT measures quantitative measurement of manual ability. The methods, however in the description of the quantitative measurement of manual ability, doesn't mention TeleCAT. It would be useful to clarify this.

(R) We agree with the reviewer that it was not clear and we have changed the MS accordingly on page 4 by adding: "…obtained using sensorized objects and Tele-UPCAT platform"

5. It would be useful to finish the background section with stating the aims of the study. They are integrated into the methods, but are more conventionally placed at the end of the introductory section.
(R) As suggested, we have integrated the introductory part of the Methods/Design at the end of the Background section on pages 3-4.

6. There is now more clarity about the parent feedback about feasibility. However the study design section focuses on a questionnaire to grade 'feelings' about proposed activities. Perhaps it might be more accurate to say the questionnaire is ascertaining parents' perception about the experiences of using Tele-CAT.

(R) We have changed the MS accordingly on page 4 to read "…ascertaining the perception about their experiences of using the Tele-UPCAT system."

7. In addition the methods section says the questionnaire is completed using a semi-structured interview which seems at odds with the multiple choice options advised in this part of the paper. Can this be made clearer and consistent?

(R) We agree and we will undertake qualitative interview with a sub- sample of participants to ascertain acceptability of: i) customization of exercises, ii) suitability of children with UCP for the Tele-UPCAT system in their own home , iii) feasibility at home, iv) required effort by the participants, v) acceptability of actigraphs, vi) suitability of the manual and vii) of the software. We will administer the questionnaire as an interview to obtain open ended questions of parents and the patients, to register also their "open" and "free" opinion about the training and the system. For more clarity, we have added the items of interview in Appendix 4.

8. Next paragraph – CONSORT in upper case

(R) We have changed this in the MS accordingly.

9. The final sentence of the Blinding section isn't clear – I can't work it out in order to provide a suggestion. If there are assessment conducted outside of the study, why would they be mentioned? Is it being suggested that assessments completed after participant withdrawal will be included in the research. Or does it mean that children can withdraw from the intervention phase but invited to continue to be involved in the ongoing study assessments?

(R) We confirm that under the ethical guidelines of the study participants are free to withdraw from the project at any time should they wish to, and there usual clinical care and monitoring by the clinical team would not be impaired. We have changed the MS accordingly on page 5.

10. The inclusion criteria related to the HFCS remains confusing. What about considering something like: House Functional Classification System score ≥2, that is, able to passively hold an object in the hand or better.

(R) We thank the reviewer for this suggestion and have changed the MS accordingly on page 5.

11. The second sentence under "Study Treatment" heading is not clear and needs to be amended.

(R) We have changed the MS accordingly by adding examples of what was implemented and requested in relation to the previous clinical experience on page 6 by adding the following sentence

"…Tele-UPCAT system (e.g. the size of the screen, the need of a guide for alternating the time of observation and of execution, the key words for catching the attention, etc), the AOT library of exercises (e.g. the adaptation of the objects for enlarging the exercises to more impaired hands) and the experimental training (e.g. time and duration) ".

12. Thank you for amending the information about inverting the images on the video. However, I am still not clear. The current description suggests that children with right UCP view an actor using their own right hand for unilateral actions, therefore they are NOT viewing a mirror image but viewing a reversed image. If this is the case, then the second last sentence is clear. The last sentence is not clear, and could read something like: For children with left UCP the same images are reversed.

(R) We have changed the MS accordingly on page 7 to read "reversed".

13. Information about the assessments is now more comprehensive and inclusion of justifications for usage outside validated age groups is responsible.
The description of the CPQOL needs to be clearer – including using correct terms. For instance it appears, but important to confirm, that the primary caregiver version was used for younger children and the teen self report version was used by older children.

(R) In both cases the primary caregiver version was used and filled in by the parents. We have changed the MS accordingly on page 11.

14. The description of the quantitative measurement during unimanual and bimanual manipulation in the outcome measures section doesn't make it clear that it is part of the TeleCAT technology or how it is part of TeleCAT.

(R) The sensorized toy and the relative set up has been designed in the context of the Tele-UPCAT project but it is out of the Tele-UPCAT system. We have better specified it in the MS on page 11 by adding "This set-up is out of Tele-UPCAT system even if it was designed and developed in parallel".

15. Statistical analysis section. "To test our first hypothesis, an intention to treat analysis will be carried out, evaluating between-group differences for primary and secondary outcome measures at the primary endpoint (T1), compared with T0, by means of parametric or non-parametric tests for unrelated samples." Please add in the words change scores in this sentence to reinforce that the difference from baseline between groups is being analysed. If change scores are not being used, then I believe the words "compared with T0" need to be deleted.

(R) We have better clarified that we are being analysing delta scores (T1-T0).

16. The next sentence needs more information about the purpose of the "exploratory analysis", what is this and how does it relate to study aims.

(R) We agree that this was not fully clear. We have planned secondary sensitivity analyses to determine if some variables (such as age or HFCS level or participant's compliance) are predictive of better responses to the Tele-UPCAT training. We have added this aim on page 12.

17. Figure 2 – schedule of enrolment etc. There are 3 horizontal arrows. I think perhaps these are not in the correct places.

(R) We think that they are actually in the correct place. The first one is for the experimental group that will perform the training between T0 and T1. The other two arrows are for the waitlist group that will perform the standard care before (first arrow) and then the experimental training (second arrow).

18. Figure 3 is a very elegant infographic which contains useful information. I believe there is too much detail to be included in either a print journal or an electronic supplementary file.

(R) We agree with the reviewer that fig.3 contains useful information and we thank her for her judgement of her elegance. For the above consideration we would like to maintain it and we have reduced some written details excluding them from the figure and including them in the description of the figure.

19. Strengths and limitations. A new issue has been raised about measurement of visual attention. I don't believe it is appropriate to raise this issue without it being addressed in the body of the protocol

(R) We have changed the limitation sentence accordingly on page 2, by adding "force and pressure hand measurements during AOT training" and on pages 6 and 7, raising this issue in the text.

I appreciate the amendment of the term "subjects" to participants – there are still instances of "subjects" and "patients" to be replaced.

(R) We have changed the MS accordingly.

Again, I look forward to seeing this really interesting protocol published and the results of the study being made available.

(R) We would like to thank the reviewer's for her interest and the useful comments that have improved our study protocol.

Reviewer: 3
Reviewer Name: Anthony Terrence O'Brien
Institution and Country: Independent, Colombia
Please state any competing interests: None declared

1. Summary
Manuscript bmjopen-2017-017819 is a protocol for an exploratory, cross-over design (waitlist), randomized clinical trial investigating the application of Action Observation Training (AOT) delivered via a new Information and Communication Technology (ICT) platform, Tele-UPCAT, in a home setting with children and young people with Unilateral Cerebral Palsy (UCP).
The main outcome is Assisting Hand Assessment, while secondary and other outcomes are: The Melbourne Assessment 2, Box and Block test, ABILHAND, Participation and Environment Measure-Children and Youth (PEM-CY) and Cerebral Palsy Quality of Life Questionnaire (CP-QoL), and quantitative reaching and grasping measurements from a sensorized object, in upper limb activities and daily life activities detected from 2 independent wrist-worn devices (Actigraphs GXT3+).
The clinicaltrial.gov registration number is NCT03094455 and the PICOT match the clinicaltrials.gov description set forth within this manuscript/protocol. This trial started on March 29, 2017 and is also the continuation of the groups prior work 1) Upper limb children action-observation training (UP-CAT): a randomized controlled trial in Hemiplegic Cerebral Palsy, 2) Randomized trial of observation and execution of upper extremity actions versus action alone in children with unilateral cerebral palsy.
The version received is a revised manuscript (already peer-reviewed), and the authors have made a very comprehensive and clear response towards the prior peer-review comments.

(R) We appreciate the positive comments of Reviewer 3.

2. Some minor aspects that they may consider are:

2. 1) Page 6, lines 7-12: To account for the large age difference the groups will be dichotomized and also categorized according to their HFCS. The sample size is derived from the group's 2 prior works, and the sample size in those projects are from Elliason et al (Effects of constraint-induced movement therapy in young children with hemiplegic cerebral palsy: an adapted model.). The concern is that due to the clustering of groups, if the sample size is adequately powered to find a significant difference for the subgroups designed within this manuscript. If it is, the authors may consider stating that it was accounted for.

(R) We have revised the MS accordingly by adding "Taking account of the study design and the stratification" for the calculation of the sample size.

2. 2) Page 7, line 29: "[…] left UCP the previous videos where tipped over if they maintained the same characteristic of the […]" Rather than tipped over, authors may consider writing that the image was horizontally flipped.

(R) According to Reviewer #2 (reply 12) we have replaced "tipped over" with "inverted".

2.3) Page 9, line 49. Remove the word "will"

(R) We have revised the MS accordingly.

2.4) Page 11-12, though ITT is the planed statistical analysis, do authors have a plan for measuring adherence or taking into account any deviations from adherence? This though not described in the clinical trials registry, and is of important when testing home based devices (well almost any intervention but more so for a trial like this). If "The age, HFCS level, characteristics of usual care (in both groups), supervision of caregiver will be analysed for further exploratory analyses" alludes to such, it could be reworded as is not clear. Also if adherence it so be measured, authors may consider describing it in the outcomes and what implications it may have on the results, and the statistical analysis. Aside, if it is also possible to include the expected clinically significant difference in the primary outcome, it would be useful for interpreting changes. Finally, as this is a relatively small trial, though the objective is to look at grouped differences, the size permits for an individual/participant based analysis, and may be worth it. A paragraph on any descriptive analysis can also be included.

(R) We have planned to assess acceptability of the Tele-UPCAT system by questionnaire (added in Appendix 4). We have added this item also in the statistical analysis section.

2.5) As there is a group which will be crossed-over, is there a wash out period or any intention to account for possible carry-over effect?

(R) Actually our study has a waitlist design (it is not a cross-over trial) with T1 as primary endpoint, so that wash out period and a carry over effect are not foreseen because after T1 the two groups will have two different ways and the data will not be merged.

2.6) Any foreseeable limitations can also be described within the protocol

(R) We have now added possible limitations such as the lack of force and pressure hand measurements during AOT training". We have changed the MS accordingly in section Tele-UPCAT system (pages 6 and 7).

2.7) Authors can make reference in text to supplementary material (already provided) which describes devices etc (eg. Actigraphs GXT3+)

(R) We have indicated the web link for having more details.

3. Overall the authors touch on the important points for carrying out a home-based device based clinical trial, i.e.: 1) ensure that there is a means of training the person in charge of administering the intervention, 2) remote monitoring of compliance by a proxy (though not in real time, it is being monitored), 3) sufficient operating procedure resources are made available to participants and families, 4) easy to use devices, 5) fixed dosing/training parameters, and 6) safety monitoring. For future trials if it is possible to have on-going/live monitoring of compliance and a protocol for discontinuation, this will benefit the trials also. Otherwise it is a thoroughly planned protocol by a group with experience in this area.

(R) We completely agree with the Reviewer and the tele-rehabilitation with a complete tele-monitoring and customization of AOT training is our dream for more extensive and more economically funded future projects.

Thank you for the opportunity to review your work and best wishes in its successful completion and future contribution.
Respectfully.
Peer-reviewer BMJ-Open

Reviewer: 4
Reviewer Name: Dr Laura Bonnett
Institution and Country: University of Liverpool, United Kingdom
Please state any competing interests: None declared

Please leave your comments for the authors below

Although I did not review the original submission, I have been pleased to review this revised version of a protocol for an RCT of home-based Tele-UPCAT for participants with unilateral cerebral palsy. The protocol is generally very good. Although the proposed methodology is brief, this is acceptable for a protocol.

The study design concerns me slightly. However, I do appreciate that it has been approved by the ethics committee. The design as it currently stands does not enable comparison of the long-term impact of Tele-UPCAT. However, it is acceptable to assess short-term outcomes by comparing the results of the control and intervention groups at 3 weeks. For this reason I will accept the design as it stands within this protocol.

(R) We appreciate the comments of the Reviewer.

VERSION 3 – REVIEW

REVIEWER	Anthony Terrence O'Brien Independent Colombia

REVIEW RETURNED	04-Nov-2017

GENERAL COMMENTS	The authors have done a thorough job responding to the peer-reviewers. I am satisfied with the protocol, my only suggestion is that they provide detail on their exploratory analysis on "age, HFCS level, characteristics of usual care (in both groups), supervision of caregiver, acceptability of therapy (measured by semi structured interview)". I assume they will use regression modeling however it is not specified (this is important as the sample size is small, and even though exploratory, multiple analysis will inflate false positive rates). However, this is left to the discretion of the authors. Nonetheless, the main objective of the protocol, its methodology, PICOT, main statistical analysis plan, and limitations are addressed. To this end, the protocol complies with the SPIRIT guidelines, and is in an acceptable state. Thank you for the opportunity to review your protocol, and to BMJ also. Respectfully.

REVIEWER	Hsiu-Ching Chiu Associate Professor Department of Physical Therapy, School of Medicine for International Students, I-Shou University, Taiwan
REVIEW RETURNED	11-Nov-2017

GENERAL COMMENTS	This protocol looks like that authors haven't done any feasibility study yet and will do with this randomised controlled trial (RCT). However, feasibility should be conducted before the randomized controlled trial. Furthermore, there are too many questionnaires in this randomized controlled trial already, so I don't think children can take all and plus other issues related to a feasibility study. It would be unfair to those participants because children would be too tired. I would suggest report result from a feasibility which is more realistic than a protocol before a randomized controlled trial.

VERSION 3 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: 3

Reviewer Name: Anthony Terrence O'Brien

Institution and Country: Independent, Colombia

Please state any competing interests: None declared

1. The authors have done a thorough job responding to the peer-reviewers. I am satisfied with the protocol, my only suggestion is that they provide detail on their exploratory analysis on "age, HFCS level, characteristics of usual care (in both groups), supervision of caregiver, acceptability of therapy (measured by semi structured interview)".

I assume they will use regression modeling however it is not specified (this is important as the sample size is small, and even though exploratory, multiple analysis will inflate false positive rates). However, this is left to the discretion of the authors.

(R) We have revised the MS accordingly by adding "…exploratory analysis (e.g. regression modelling) in order to…" in the Statistical analyses Section.

Nonetheless, the main objective of the protocol, its methodology, PICOT, main statistical analysis plan, and limitations are addressed. To this end, the protocol complies with the SPIRIT guidelines, and is in an acceptable state.

(R) We appreciate the positive comments of Reviewer 3.

Thank you for the opportunity to review your protocol, and to BMJ also.

Respectfully.

Reviewer: 1

Reviewer Name: Hsiu-Ching Chiu

Institution and Country: Department of Physical Therapy, School of Medicine for International Students, I-Shou University, Taiwan

state any competing interests: None

1. This protocol looks like that authors haven't done any feasibility study yet and will do with this randomised controlled trial (RCT). However, feasibility should be conducted before the randomized controlled trial. Furthermore, there are too many questionnaires in this randomized controlled trial already, so I don't think children can take all and plus other issues related to a feasibility study. It would be unfair to those participants because children would be too tired. I would suggest report result from a feasibility which is more realistic than a protocol before a randomized controlled trial.

(R) As already replied to Reviewer #1, in the previous submission we aim to run a pilot (indicated as exploratory) RCT study that according to literature [e.g. Feeley et al., et al (2009). The importance of piloting an RCT intervention. Canadian Journal of Nursing Research, 41(2), 84–99] is the best option to test the feasibility of the features of a RCT, and as such requires random assignment of participants to a group. This type of study allows us to assess both the feasibility and acceptability of the intervention and its design and procedures. We do not believe the children will be too tired as we have performed these studies with the same design and number of measures and have had very high compliance rates. In the event of any issues these will be recorded, as proposed in our study protocol using the best experimental design (pilot RCT) as recommended in the literature.

VERSION 4 – REVIEW

REVIEWER	Hsiu-Ching Chiu Associate Professor Department of Physical Therapy, School of Medicine for International Students, I-Shou University
REVIEW RETURNED	02-Jan-2018

GENERAL COMMENTS	**Comments**

General comments

Overall, this paper is well-written and understandable. However, there are some omissions, such as missing figure 1, figure 2, figure 3 and 4, lack argument of the content of introduction. Major revision is required to make for the introduction. Some minor remediation of written problems would make this paper be easier to follow, suggesting authors go through the whole paper for the readability before the next submission. Specific details are as below:

Abstract.

1. Introduction:
   1st sentence-UCP is required to "Unilateral cerebral palsy (UCP)", because this is first place to show this abbreviation.

2. Method and Analysis:
   (1) 3rd sentence-Please change to "The control group will receive usual care for 3 weeks which may have included upper limb training. They will be offered AOT at home after 3 weeks."
   (2) 4th sentence- please change to "Twenty-four children with UCP will be recruited for 12 participants per group. The primary outcome will be measured using…."
   (3) 5th sentence- place replace" subject" to "participants".

Strength and limitation of this study.

-Second point- please delete "a clinical population of"

-third point- please change to "….the different levels of upper limb severity…"

-4th point= please change to "…even if it will be calculated and powered.."

Introduction-content-First paragraph

1. First paragraph is too long. This is required to break into 2

	paragraphs. 2. Second sentence- Please add a reference in this. 3. Third sentence- Please add "….(….impacting the body more than the other side)"… 4. There is lack of literature review, because current clinical practice is constraint induced movement therapy which is not mentioned in the introduction. Also, there are some studies about bimanual intervention. Authors need to give strong evidence why this AOT is potential for the improvement. Also, why authors think the disadvantage of other therapies and this AOT can conquer others. **Introduction-content-Second paragraph-page 4 (small points)** 1. Please delete "be to", so the sentence will be" The primary aim will evaluate…." 2. Third line- please delete "to", so the sentence will be "and assess whether…." **Introduction-content-third paragraph (small points)** 1. Please delete " be to" in the first sentence. 2. Second sentence- Please change to "Further aims will assess the feasibility of …." **Methods: Study design** 1. Second sentence- Please change to "This study is…" 2. Second paragraph- It's difficult to understand the first sentence, please re-write. 3. I cannot see Figure 1, 2, 3, 4 in this manuscript, did authors forget to upload? **Methods: Blinding** 1. First paragraph, last sentence- Please add "," after During the assessment, 2. Second paragraph, first sentence- Please change to "(two paediatric neurologists)" 3. Second paragraph, second sentence- Please change to "), the retention of participants in each study arm and the compliance of study protocol…." 4. Second paragraph, third sentence- Please change to "Each participant will have.." 5. Second paragraph, fourth sentence- Please change to "The file with participant's numbers…" 6. Second paragraph, sixth sentence- Please delete "of when expected" 7. Second paragraph, last sentence- Please change to "…from this study any time and have been notified that their …." **Methods: Study sample and recruitment** 1. First paragraph, first sentence- Please change to "….by paediatric neurologists…."

	2. Last sentence- Please change to "…within 6 months prior to the enrolment of this study." **Methods: Sample size** Suggest change first sentence to "Even if this study will be planned as…." **Methods: Study treatment** 1. Second last sentence-Please use 1 hour to replace 60 minute. 2. Last sentence- Please change to "Three different actions will be proposed twice each day" 3. This part is a bit overlapping with experimental training. I am wondering if it is possible to combine these two sections. **Methods: Experimental training** Does experimental group receive standard care? If so, please provide dose. **Methods: standard care** Please provide information about dose, because it is important.

VERSION 4 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: 1

Reviewer Name: Hsiu-Ching Chiu

Institution and Country: Associate Professor

Department of Physical Therapy, School of Medicine for International Students, I-Shou University, Taiwan

State any competing interests: None declared

Overall, this paper is well-written and understandable. However, there are some omissions, such as missing figure 1, figure 2, figure 3 and 4, lack argument of the content of introduction. Major revision is required to make for the introduction. Some minor remediation of written problems would make this paper be easier to follow, suggesting authors go through the whole paper for the readability before the next submission. Specific details are as below:

Abstract

1. Introduction:

1st sentence-UCP is required to “Unilateral cerebral palsy (UCP)”, because this is first place to show this abbreviation.

(R) We have changed as suggested

2. Method and Analysis:

1. 3rd sentence-Please change to “The control group will receive usual care for 3 weeks which May have included upper limb training. They will be offered AOT at home after 3 weeks.”

2. 4th sentence- please change to “Twenty-four children with UCP will be recruited for 12 participants per group. The primary out come will be measured using.”

3. 5th sentence- placereplace” subject” to “participants”.

(R) All the three sentences have been changed accordingly to Reviewer’s suggestions

Strength and limitation of this study.

-Second point- please delete “a clinical population of”

-third point- please change to “….the different levels of upper limb severity…”

-4th point= please change to “…even if it will be calculated and powered..”

(R) All the suggested sentences have been changed accordingly to Reviewer’s suggestions

Introduction-content-First paragraph

1. First paragraph is too long. This is required to break into 2 paragraphs.

(R) We have divided the first paragraph in more paragraphs.

2. Second sentence- Please add a reference in this.

(R) We have added the following reference:

Surveillance of Cerebral Palsy in Europe. Surveillance of cerebral palsy in Europe: a collaboration of cerebral palsy surveys and registers. Surveillance of Cerebral Palsy in Europe (SCPE). Dev Med Child Neurol 2000;42(12):816-24.

3. Third sentence- Please add “….(….impacting the body more than the other side)”…

(R) We have changed as suggested

4. There is lack of literature review, because current clinical practice is constraint induced movement therapy which is not mentioned in the introduction. Also, there are some studies about bimanual intervention. Authors need to give strong evidence why this AOT is potential for the improvement. Also, why authors think the disadvantage of other therapies and this AOT can conquer others.

(R) We have modified the Introduction section adding some reviews on the use of CIMT and HABIT. Our aim and hypothesis are not to demonstrate that AOT is better than the others therapies (this would have had required a comparative study) but that AOT is an effective model for upper limb treatment and that this model of treatment can also delivered at home thanks to ICT technologies. We have added this point in the discussion.

Introduction-content-Second paragraph-page 4 (small points)

1. Please delete “be to”, so the sentence will be” The primary aim will evaluate….”

2. Third line- please delete “to”, so the sentence will be “and assess whether….”

(R) We have changed as suggested

Introduction-content-third paragraph (small points)

1. Please delete “ be to” in the first sentence.

2. Second sentence- Please change to “Further aims will assess the feasibility of ….”

(R) We have changed as suggested

Methods: Study design

1. Second sentence- Please change to “This study is…”

(R) We have changed as suggested

2. Second paragraph- It’s difficult to understand the first sentence, please re-write.

(R) We have re-written the sentence

3. I cannot see Figure 1, 2, 3, 4 in this manuscript, did authors forget to upload?

(R) We do not know what happened because all the Figures were uploaded and they were present in the pdf that we approved before the submission

Methods: Blinding

1. First paragraph, last sentence- Please add "," after During the assessment,

2. Second paragraph, first sentence- Please change to "(two paediatric neurologists)"

3. Second paragraph, second sentence- Please change to "), the retention of participants in each study arm and the compliance of study protocol…."

4. Second paragraph, third sentence- Please change to "Each participant will have.."

5. Second paragraph, fourth sentence- Please change to "The file with participant's numbers…"

6. Second paragraph, sixth sentence- Please delete "of when expected"

7. Second paragraph, last sentence- Please change to "…from this study any time and have been notified that their …."

(R) We have changed all the previous sentences as suggested

Methods: Study sample and recruitment

1. First paragraph, first sentence- Please change to "….by paediatric neurologists…."

2. Last sentence- Please change to "…within 6 months prior to the enrolment of this study."

(R) We have changed as suggested

Methods: Sample size

Suggest change first sentence to "Even if this study will be planned as…."

(R) We have changed as suggested

Methods: Study treatment

1.Second last sentence-Please use 1 hour to replace 60 minute.

(R) We have changed as suggested

2. Last sentence- Please change to "Three different actions will be proposed twice each day"

(R) We have changed as suggested

3. This part is a bit overlapping with experimental training. I am wondering if it is possible to combine these two sections.

(R) These two parts in the Ms of our first submission (May 2017) were combined and it was suggested by the Reviewers to split adding a general part at the beginning. Therefore, at this point we would prefer to maintain these sections separately.

Methods: Experimental training

Does experimental group receive standard care? If so, please provide dose.

(R) The experimental group will proceed with their “traditional” rehabilitative program (standard care) and the therapies will be registered in the daily diary. This point is indicated in the sentence at the end of “standard care” paragraph (“The frequency and the type of all therapies will be recorded accurately by a diary in both groups.”). We have added a line space to split this sentence from the standard care paragraph.

Methods: standard care

Please provide information about dose, because it is important.

(R) We agree with the reviewer that the dose is important and we will register the dose of standard care in both groups thanks the diary. We have added “dose” in the sentence mentioned above: “The frequency, dose and the type of all therapies will be recorded accurately by a diary in both groups”.

VERSION 5 – REVIEW

REVIEWER	Hsiu-Ching Chiu Associate Professor Department of Physical Therapy, School of Medicine for International Students, I-Shou University, Taiwan
REVIEW RETURNED	20-Feb-2018

GENERAL COMMENTS	I am satisfied with all changes, but I still cannot see Figure 2, 3, and 4. There are two things about references which editors can decide. 1) Reference in text, it should be uppercase letter. 2) Reference list, I am wondering if authors should delete something like "doi: 10.1016/j.jval.2015.09.683. "