Author's response to reviews

Title: Instrumented gait analysis and individually tailored interdisciplinary interventions for children with cerebral palsy: A randomised controlled trial protocol

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Author's response to reviews: see over
The use of Instrumented gait analysis for individually tailored interdisciplinary interventions in children with cerebral palsy: A randomised controlled trial protocol

Enclosed please find a revised version of the above manuscript. We have carefully addressed and tried to answer all questions raised by the reviewers, which we believe has significantly improved the quality of the manuscript. A detailed point-to-point list of our replies to the questions raised and the corresponding changes made in the manuscript is seen below together with the submission of the revised manuscript. All parts in the text that have been modified are described in the below point-by-point response.

On behalf of all Authors

Helle Mätzke Rasmussen
Major Compulsory revisions

Reviewer 2, comment 1: One major concern I have, relates to the standardisation of the interventions. To what extent will these be standardized? Are they described in a protocol (how and what to do exactly both when information of IGA is provided and when not) and will people be trained to perform the interventions? Or is it up to the therapist/surgeon to decide what to do? Standardization (at least to so some part) and training seem important since the interventions will be performed in 26 difference settings.

Author’s reply: The question about standardisation of the interventions is addressed in both this proposal for a major compulsory revision and in a proposal for minor essential revision (reviewer 2, comment 20). The question about standardisation of the interdisciplinary intervention concerns all trials with a ‘pragmatic approach’. The present study aims to investigate effects of the two interventions modalities in a ‘real clinical context’.

Consequently, a standardized, controlled environment is not feasible. It has, as reviewer 3 all so point out, been challenging to articulate the crux of the study, but we believe that the present revised version will provide the reader and reviewers with sufficient information and knowledge to understand that the pragmatic approach is correct for this particular study.
Minor essential revisions

Reviewer 1: Elena Gutierrez-Farewik

Intervention

Reviewer 1, comment 1 (page 7): the authors describe IGA and impairment-focused interpretation as an intervention (p7) in itself (it is not an intervention)

Author’s reply: we understand that the description may be perceived as such and have made the following changes in the section.

Revised text, page 8, line 172-174: The experimental intervention will include individually tailored interdisciplinary intervention based on clinical examinations, standardised measurements of walking and recommendation of interventions based on knowledge about the impairments that affects the gait from IGA.

Intervention and differences between groups

Reviewer 1, comment 2: Who will decide the interventions performed in the ‘care as usual’ group? Assuming the interdisciplinary gait lab group will only be involved in treatment decision making in the IGA group, then the study will evaluate this group’s treatment-recommendation skills rather than the added benefit of IGA. The authors do bring this up (that they really are testing the effectiveness of two different treatment paradigms on gait improvement in CP), but will the difference be due to IGA+impairment-focused interpretation, or due to a more or less experienced/skilled/risk-taking group recommending the interventions? This point could be made a bit clearer.

Author’s reply: As stated in the discussion section (page 15, line 363-365), “... the current trial is not designed to distinguish between the different elements in the two intervention groups...”. Nevertheless, this can be highlighted in the methods section, where we have made the following addition.
Revised text, page 7, line 154-155: The trial is not designed to distinguish between the different elements in the two intervention groups.

Participants

Reviewer 1, comment 3 (page 6, line 140-141): The authors also only include children in GMFCS levels I and II, which represents a reasonably motor well-functioning subgroup of children with CP. This point could be made clearer and repeated in the hypotheses. Why did the authors only choose this group?

Author’s reply: The GMFCS levels of the participants are already stated in the hypotheses, but the following clarification has been added to the discussion section.

Revised text, page 16, line 382-384: To ensure good quality in data from IGA participants at GMFCS I and II have been chosen. However, this may impact the generalisability of findings.

Reviewer 1, comment 4: The title could be better. It is unclear from the title that all children will received an individually-tailored interdisciplinary intervention, but that it will be either be based on usual clinical exams or usual clinical exam + IGA.

Author’s reply: Reviewer 1 (comment 4) and reviewer 2 (comment 1) have proposed changes to the title. We agree that the suggested small changes in the title might ensure a better understanding of the two modalities of intervention under investigation.

Original text: Instrumented gait analysis and individually tailored interdisciplinary interventions for children with cerebral palsy: A randomised controlled trial protocol

The revised text: The use of Instrumented gait analysis for individually tailored interdisciplinary interventions in children with cerebral palsy: A randomised controlled trial protocol.
Reviewer 2: Merel Brehm

Title

Reviewer 2, comment 1: Suggestion for revising: Instrumented gait analysis for individually tailored interdisciplinary interventions in children with cerebral palsy: A randomised controlled trial protocol.

Author’s reply: Reviewer 1 (comment 4) and reviewer 2 (comment 1) have proposed changes to the title. We agree that the suggested small changes in the title might ensure a better understanding of the two modalities of intervention under investigation.

Original text: Instrumented gait analysis and individually tailored interdisciplinary interventions for children with cerebral palsy: A randomised controlled trial protocol

The revised text: The use of Instrumented gait analysis for individually tailored interdisciplinary interventions in children with cerebral palsy: A randomised controlled trial protocol

Length of the abstract

Reviewer 2, comment 2: General: rather lengthy abstract.

Author’s reply: We recognize that the abstract is quite long and has shortened the abstract (from 341 words to 297 words), where it has been possible.

CP follow-up program

Reviewer 2, comment 3 (page 1, line 25): From the text is does not become clear what is meant with the ‘CP follow-Up Program’. A clarification would be helpful for the reader.

Author’s reply: We acknowledge that ‘CP follow-up Program’ is not clearly defined in abstract, therefore we have chosen not to use the term in the abstract after the general revision and shortening of the text.
Language changes

Reviewer 2, comment 4 and 5 (page 2, line 29 and 32): ...result in improved gait pattern… should be: result in an improved gait pattern and line 32 … to those in ‘care as usual’...

Author’s reply: We agree that these changes will improve our manuscript. The first part of the original text (line 29) has been removed from the abstract in the general shortening of the abstract and the second part has been changed (line 32).

Revised text, page 2, line 27-29: The aim of this study is to test the hypothesis that improvements in gait following individually tailored interventions when IGA is used is superior to those following ‘care as usual’.

Care as usual

Reviewer 2, comment 6 (page 2, line 32 + 38): what is meant with ‘care a usual’? Is that any interdisciplinary individually tailored interdisciplinary intervention addressing impairments though not identified by instrumented 3-dimensional gait analysis? Please clarify. From the abstract it does not become clear.

Author’s reply: After the general revision of the abstract the description on ‘care as usual’ have been clarified.

Revised text, page 2, line 23-26: Children with cerebral palsy (CP) often have an altered gait. Orthopaedic surgery, spasticity management, physical therapy and orthotics are used to improve the gait. The Interventions are individually tailored and are planned based on clinical examinations and standardised measurements to assess walking (‘care as usual’)…

Instruments for assessing secondary outcome measures

Reviewer 2, comment 7 (page 2, lines 39-40): Information on the instruments/tests for assessing the secondary outcome measures should be provided (between brackets).
Author’s reply: After a general shortening of the abstract is has become possible to add the instruments, which are used for assessing the secondary outcome measures.

Revised text, page 2, line 34-38: Secondary outcome measures are, walking performance (1-minute walk test) and patient-reported outcomes of functional mobility (Pediatric Evaluation of Disability Inventory), health-related quality of life (The Pediatric Quality of Life Inventory Cerebral Palsy Module) and overall health, pain and participation (The Pediatric Outcome Data Collection Instrument).

Language changes

Reviewer 2, comment 8: Page 3, line 66: remove ‘their’ from the sentence.

Author’s reply: We agree that these changes will improve our manuscript and have removed ‘their’ from the sentence.

Clinical decision-making and value / relevance of current study

Reviewer 2, comment 9 (page 3, lines 70-71): The relevance of identifying features in the gait pattern reflecting underlying neuro-musculoskeletal impairments with IGA is not described’. E.g. is IGA expected to (better) guide clinical decision-making compared to the information gained from the GMFCS, GMFM and FMS? This should be addressed.

Reviewer 2, comment 12 (page 4, in lines 87-89): it is stated: However, whether interdisciplinary interventions directed towards impairments identified by IGA in children with CP result in improvements in the gait pattern compared with ‘care as usual’ without IGA has not been investigated. It seems that Lofterod (reference 19) also compared the results of treatment on gait when following gait-analysis recommendations in children with CP. What is the added value/relevance of the current study? This should be stated more convincingly.

Author’s reply: We appreciate that the reviewer have brought this to our attention and acknowledge that the original manuscript might not have made it clear, the value of adding
IGA to the current practise (‘care as usual’) and thus the clinical relevance of the current study. Therefore, we have elaborated on the use of IGA, the differences between the two interventions and the relevance of the study in following sections to the manuscript.

Revised text, page 4, line 79-82: The use of IGA makes it possible to make clinical decision regarding individually tailored interventions based on clinical examination, standardised measures and recommendation of interventions from IGA, in contrast to the current practice (‘care as usual’) where only clinical examinations and standardised measures are used.

Page 4, line 85-95: The effects of individually defined physiotherapy in children with cerebral palsy based on clinical examination and IGA have been investigated in a prospective double blind cross over study [1]. The authors observed a superior effect of individually defined physiotherapy on achievement of treatment goals, gross motor function and some selected gait parameters compared with a generic training program. The use of IGA per see has only been investigated in relation to decision-making in orthopaedic surgery and effects of individually defined physical therapy.

To our best knowledge, the potential added benefit of using IGA in the decision making of interdisciplinary interventions directed towards impairments in gait has not been investigated in children with CP. Thus, a study investigating potential difference in improvements in overall gait pathology following individually tailored interdisciplinary intervention with or without IGA is needed.
Length of description of IGA

Reviewer 2, comment 10 (page 3/4, lines 73-78): Somewhat lengthy description of IGA.

Author’s reply: We recognize that the description is quite long and has shortened the length of the section by approximately 1/3.

Revised text, page 4, line 71-74: The purpose of IGA is to provide objective and valid measures of gait in three planes [2]. With the use of infrared camera technology and force plates embedded in the floor, it is possible to determine joint movement (kinematics), joint torque and power (kinetics) and tempo-spatial parameters. IGA thus provides a large amount of interdependent data and variables corresponding to different gait pathologies.

Language changes; gait indices

Reviewer 2, comment 11: Page 4, lines 81-83: suggestion for revising: For example, the gait Deviation Index (GDI) and Gait Profile Score summarize the overall gait pathology into a single score for each patient, whereas Gait Variable Score…

Author’s reply: We agree that these changes will improve our manuscript and have revised the sentence as recommended.

Revised text, page 4, line 75-78: The quantity and complexity of data have led to the description of different indices that quantify a part of or the overall gait pathology into a single score. For example, the Gait Deviation Index (GDI) [3], and Gait Profile Score [4] summarise the overall gait into a single score for each patient, whereas Gait Variable Score is an index for a single gait variable rather than a single score for all variables [4].

Description of the aim of the study

Reviewer 2, comment 13 (page 4, line 90): suggestion for revising: ….which of the two modalities (i.e. interdisciplinary intervention directed towards impairments identified with or
without IGA)….etc.. In addition, when changing the text as such, the following sentence can be removed: line 93: The two modalities differ in the use of IGA.

Author’s reply: We agree that the proposed revision will improve the manuscript and have implemented it into the manuscript.

Revised text, page 4, line 95 – page 5, line 99: The aim of this study is to determine which of two modalities (i.e. individually tailored interdisciplinary intervention with or without IGA) leads to greater improvements in the overall gait pathology, walking performance and patient-reported outcomes of functional mobility; overall health, pain and participation in normal daily activities and health-related quality of life after 52 weeks.

Overview of the two modalities

Reviewer 2, comment 14: Page 4, in lines 93-95 it is stated: An overview of the two modalities of individually tailored interdisciplinary interventions is described in Figure 1. This information should not be part of the purpose statement of should be described in the methods section.

Author’s reply: The information is already part of the methods section (page 6, line 124). Based on the reviewer comment, we have decided to remove the information from the purpose section.

Primary and secondary hypothesis

Reviewer 2, comment 15: Page 5, line 99: Suggestion for revising: The use of IGA when prescribing individually tailored interdisciplinary interventions…. Similar suggestion for the secondary hypothesis.

Author’s reply: We do agree that the wording of the primary and secondary hypothesis can be improved and have made the following revisions.
Revised text, page 5, line 103 and 108: The use of IGA in the planning of individually tailored interdisciplinary intervention will…

Methods section

Reviewer 2, commend 16: General: lengthy description of the methods section.

Author’s reply: We recognize that the method section is quite long and has shortened the section, where is has been possible.

Language changes

Reviewer 2, comment 17 (page 5, lines 116-119): suggestion for revising/condensing: A prospective, single blind, parallel group, balanced randomisation [1:1] study will be conducted, performed in accordance with guidelines of the CONSORT statement [20, 21].

Author’s reply: We agree that these changes will improve our manuscript and have revised the sentence as recommended.

Participants

Reviewer 2, comment 18: Page 6, line 131: was there a specific reason for the small age range for children (5-8) in term of the applicability of IGA in children aged 5 and generalizability of the results to older children?

Author’s reply: The following sentence has been added.

Revised text, page 17, line 381-382: The relatively young age group have been chosen, to ensure inclusion of children at an early age, before the development of extensive and fixed deformities, that causes impairments and thus gait pathology [5].

Setting

Reviewer 2, comment 19 (page 6, line 139): Will the IGA only be performed in one center (the Motion Analysis Laboratory at Odense University Hospital)? How practical that for patients?
Author’s reply: The IGA are all performed at the same centre at Odense University hospital, since it is the only gait lab in the area of inclusion, which makes it necessary for the participants to travel to the centre. We recognize that the distance of up to 350 km may influence participation. But experiences from a previous reliability study [6], that most of the parents do not see the distance as a barrier for participation.

Standardisation of interventions

Reviewer 2, comment 20: Page 7, lines 155-163: To what extent will the interventions be standardized? Are they described in a protocol (how and what to do exactly, etc.) and will people be trained to perform the interventions? Standardization and training is important since the interventions will be performed in 26 difference settings. This should be addressed/described as such in the study and manuscript.

Author’s reply: There will be no standardisation of the interventions or training of the involved healthcare professionals, since we want to conduct a pragmatic trial, which reflect current practice. This should be stated clearly in the manuscript and therefore we have added the following to the method section.

Revised text, page 7, line 167 – page 8, line 170: The study will not be involved in the application of the interdisciplinary intervention and will not provide training or standardisation of the interventions provided by the involved hospitals and municipalities. This is done to ensure a pragmatic approach to reflect common practice and ensure high external validity of the study.

IGA Protocol

Reviewer 2, comment 21 (page 7-9): rather lengthy description of the IGA protocol. This should be condensed.
Author’s reply: We recognize that the description is rather lengthy and has shortened the section, where is has been possible.

Follow-up period

Reviewer 2, comment 22: Page 9, line 210: For all interventions, a follow up period of 52 weeks is chosen. For surgery and BTX this seems appropriate. However, for orthoses and physical therapy, effects may be present earlier (and they may even disappear over time (e.g. because of growth). For that reason, why not incorporate a gait analysis and 1-minute walk test assessment at 26 weeks?

Author’s reply: The follow up period have been discussed extensively. It has been difficult to determine the perfect timing of the follow up. Some effects might present earlier than other, but the overall aim of the interventions for children with CP often are improvement in the long term, i.e. by improving the ability to improve further or to prevent decline. Another reason not to apply the 1-minut walk and IGA at 26 weeks is that it requires attendance at the Gait Analysis laboratory at Odense University hospital, which might not be feasible, as mentioned by reviewer 2 in comment 19.

Description of outcome measure

Reviewer 2, comment 23: Page 9-12, Measurement: very lengthy description of the outcome measures. This should be condensed.

Author’s reply: We recognize that the description is rather lengthy and has shortened the abstract, where is has been possible.

Kinetic data

Reviewer 2, comment 24 (page 10, line 229): from the IGA gait cycles, kinematic data, and spatio-temporal parameters will be derived. Why not kinetic data? For clinical decision-making this information will also be useful.
Author’s reply: Unfortunately, the kinetic data was missing in the description and have therefore been added it to the text.

Revised text, page 9, line 189-191: …will be used for data processing, to define gait cycles, spatio-temporal parameters, kinematic and kinetic data [7].

Adverse events

Reviewer 2, comment 25 (page 13, lines 307-312): adverse events are reported. Could some examples of adverse events (per intervention) be given in the text?

Author’s reply: Based on the comment, we have chosen to add a sentence on potential adverse events in the section.

Revised text, page 13, line 314 – page 14, line 316: Adverse events may occur as a direct result of the study activities, such as fall during the IGA or indirectly as a result of the interdisciplinary interventions, such as pressure scores after casting.

Sample size

Reviewer 2, comment 26 (page 14, line 318): How realistic is the 10% change based on Schwartz et al, as found in diplegic children with CP, aged 3.1 to 43.3 years, who only underwent orthopedic surgery, compared to the children in the current study (GMFCS I and II, aged 5-8, and undergoing different types of interventions)?

Author’s reply: For sensitivity reasons as also stated earlier we have chosen GDI as primary outcome, therefore the sample size calculation should be based on minimal clinical important differences (MCID) specified for GDI. Different methods to determine MCID have been proposed. It is widely accepted that a patient-centred approach to determine the MCID is the anchor based method. This work has not been done for GDI. Therefore we have chosen to use the 10% proposed. Furthermore for a scientific purpose, we should not include assumptions whether it is realistic to achieve a 10% difference. However, we do believe and
hypothesize that our approach to the intervention will produce clinical relevant and statistical differences between the two interventions.
Reviewer 3: Claire Kerr

Interdisciplinary intervention

Reviewer 3, comment 1 (page 3, lines 66-73): The authors need to define what they mean by ‘interdisciplinary intervention’. Does this mean the four services outlined (surgery, spasticity management, physio and orthotics) all work independently based on the findings of individual examinations (or a centrally available examination report such as CPUP or IGA)? Do these disciplines discuss the case together? Do they refer to one another? Is this client-centred – are the child and family involved in any of these care or service provision decisions? These details are important and adequate description of the service model is required as different regions have different names for the same processes.

Author’s reply: We do agree that a more detailed description of the ‘interdisciplinary intervention’ will improve our manuscript. Therefore we have made some changes to the manuscript, however a thorough description of how the ‘interdisciplinary interventions’ are planned and implemented are not possible, because we have chosen a ‘pragmatic design’, which allows for small differences between the local teams involved in the study.

Revised text, page 3, line 60 - 68: In Denmark a patient-centred and evidence-based approach is pursued. An adapted version of the Swedish Cerebral Palsy follow-up Program is used, where the healthcare professionals use standardized examinations of the child throughout childhood [8]. A local team, which usually consists of a paediatrician, a paediatric orthopaedic surgeon and a physiotherapist, are responsible for the follow-up and individually tailored interdisciplinary interventions for each child with CP. The local team meets with the child and family once or twice a year to examine the child’s development and to plan and coordinate common goals and interventions for the child. As part of the Cerebral Palsy follow-Up Program, the overall gross motor function and walking performance are evaluated
by standardised measures such as the GMFCS, the Functional Mobility Scale and sometimes the Gross Motor Function Measure (GMFM) [9-11].

**Start of intervention**

*Reviewer 3, comment 2: Page 4, Line 93-98* The authors highlight on page 4, paragraph 2, that IGA is an important investigation for children with CP, and provide several references that demonstrate the effect IGA has on planned orthopaedic surgery in children with cerebral palsy. Thus the impact of IGA on one element of the ‘interdisciplinary intervention’ appears to be established already. The surgical emphasis is echoed by defining the ‘start of intervention’ as the date of the most invasive intervention (and within 26 weeks of baseline). To truly reflect the uptake of IGA recommendations on all four ‘interdisciplinary interventions’ (as opposed to measuring the effect of surgery etc) then I would suggest that the ‘start of intervention’ occurs when the report is released – that is when the IGA report can be taken into account in service planning. Justification for the decision of the ‘start of intervention’ is required. Additionally, even with the current delayed ‘start’ (presumably to permit scheduling of more invasive interventions) you might consider an 18 month follow up as well. It is my understanding (and experience) that many children are typically just achieving their pre-surgical functional gait capacity at 12 months post-op.

*Author’s reply:* We agree that the proposed change in definition of ‘start of intervention’ will improve our study design, and therefore as suggested, altered the ‘start of intervention’ to occur when the report is released. However, as we anticipate most of the interventions to be non-surgical and invasive to a minor degree we believe that the follow-up should be 12 months post start of intervention as initially stated. To acknowledge, that more invasive interventions might have a longer planning phase (i.e. consideration, involvement of patient
and family and finally planning of surgery) an additional follow-up 52 weeks after surgery will be conducted and a per protocol analysis will be performed.

Revised text, page 10, line 219-224: The time point ‘start of intervention’ is defined as the week where the report is released. The data collection in the control group will be adjusted according to the planned time points in the experimental group. Furthermore, to acknowledge that surgery might be influenced by a long planning phase (i.e. consideration, involvement of patient and family and planning of surgery) and rehabilitation a second post intervention examination will be performed at 52 weeks post operation and included in a per protocol analysis.

Description of gait outcome measure

Reviewer 3, comment 3 (page 9-12): The description of gait outcome measures is muddled at times (GDI, GPS and GVS). It is important to be clear as to what the GDI is – ‘a multivariate measure of overall gait pathology’ (Schwartz & Rozamulski 2008), not a ‘gait pattern’. The gait measures need to be clearly articulated and then consistently applied in the measures, exploratory measures and discussion section.

Reviewer 3, comment 5 (page 5, line 226): remove ‘gait pattern’ and replace with ‘gait deviation index’ (GDI is not gait pattern).

Author’s reply: In both literature and clinical practice a variety of terms are used to describe the specific pattern of movement during walking. In our manuscript we chose to use the term ‘gait pattern’, which is in accordance with the term “gait pattern function” in the ICF. We do however acknowledge that the term is not in accordance to the term ‘overall gait pathology’ that is used in the original article describing the development of GDI. Therefore we have changed the term ‘gait pattern’ to ‘overall gait pathology’ or ‘gait pathology’. Furthermore we have reviewed the use of the term ‘gait pattern’ and corrected the use, where we found it
reasonable. Furthermore the description of gait outcome measure has been revised to meet
the comment from the reviewer.

Cross-Contamination and non-compliance

Reviewer 3, comment 4 (page 5, lines125-128): I personally feel that the greatest risk is
contamination of the ‘care as usual’ group, however perhaps a little description on how
services are typically configured for children in the region would allay some reader concerns
about cross-contamination and potential non-compliance.

Author’s reply: We have changed the description of the health service in Denmark in the
Background section based on reviewer 3, comment 1, which hopefully will reduce the readers
concerns about cross-contamination and potential non-compliance.

Gait Deviation Index and Gait Profile Score

Reviewer 3, comment 5 (page 5, line 226 (continued): … Also provide some comment as to
why GDI was selected rather than Gait Profile Score (especially given the background and
description of ‘individualised’ approach for both control and experimental group subjects).

Author’s reply: We agree, and have added the following section to the discussion section in
the manuscript.

Revised text, page 19, line 430-432: GDI was chosen as primary outcome rather than GPS,
because the GDI compared to GPS seems to be more sensitive to change in children with a
relatively mildly affected gait [4], as expected with the study population of children at
GMFCS level I and II.

Pediatric Evaluation of Disability Inventory (PEDI)

Reviewer 3, comment 6, (page 11, line 255): clarify in the text if you plan to use the PEDI or
the PEDI-CAT (the new online version). The last sentence of this paragraph (lines 259-261)
should be deleted, as it is not relevant to the Mobility Scale of the PEDI.
Author’s reply: Thank you for drawing our attention to this. We’ve added ‘original’ and a reference to the original version. Furthermore we have removed the last sentence.

Revised text, page 12 line 262-263: The Mobility Scale of the original Pediatric Evaluation of Disability Inventory evaluates the child’s functional mobility in everyday activities with regard to functional skills and caregiver assistance [12].

**Patient satisfaction**

Reviewer 3, comment 7 (page 15, line 350): remove ‘patient satisfaction’ or replace with terms that more closely reflect the outcomes being assessed in this study.

Author’s reply: Thank you for drawing our attention to this term. It has been replaced with the terms used in the rest of the manuscript.

Revised text, page 15, line 356-358: However, its effectiveness regarding gait pathology, walking performance and patient-reported outcomes of functional mobility; overall health, pain and participation in normal daily activities as well as health-related quality of life have never been investigated.

**Exploratory outcome measures**

Reviewer 3, comment 8 (page 12, line 227): Exploratory outcome measures

This section is very muddled. The Gait Variable Score section needs to be described properly – highlighting what GVS and GPS are, how they differ from GDI, and why it would be relevant to look at them in an exploratory way. See points 3 and 5 also

Author’s reply: The description has been revised to the following

Revised text, page 10, line 225-228: In addition to the baseline data and classification, primary and secondary outcome measures, a range of exploratory outcome measures are collected. The primary and the secondary outcome measures will be used to confirm or reject the described hypotheses, while the explorative outcome measures will be used for
hypothesis generation, and to report other potential beneficial or harmful effects of the interventions.

Revised text, page 12, line 283-286: Data from the IGA will be used to calculate the median Gait Variable Score of the first five trials for each leg at a self-selected walking speed and at matched (pre and post) walking speed, to identify changes in gait pathology at joint levels. The explorative outcome measures based upon GVS will be used for hypothesis generation purposes.

**Recruitment of participants**

**Reviewer 3, comment 9 (page 16, line 369-73):** I do not see how participating in this study will ‘encourage attendance’ in CPUP, which is the type means of review in the region. Please consider removing this statement and consider revising the remainder of this paragraph for clarity.

**Author’s reply:** We agree and have modified the text, to explain that we believe that the cerebral palsy follow-up program can support the recruitment into the study.

Revised text, page 17, line 376-381: The study will be carried out in the Region of Southern Denmark and the North Denmark region. Participants will be recruited through the local teams in the cerebral palsy follow-up program, and will encourage attendance among eligible children. The cerebral palsy follow-up program makes it possible to gain information to make a thorough description of the ‘reach’ of recruitment of participants into the population of interest and to document potential study composition differences across the stages of the trial [13].

**Explorative hypothesis**

**Reviewer 3, comment 10 (page 5, line 110):** Suggest you omit ‘explorative hypotheses’ – appears very speculative
Instrumented gait analysis and individually tailored interdisciplinary interventions for children with cerebral palsy: A randomised controlled trial protocol

**Author’s reply:** We agree that the ‘explorative hypotheses’ might appear speculative. The explorative hypotheses have been changed to a phrase explaining that we will perform explorative analyses on the explorative outcomes.

*Revised text, page 5, line 115-116:* Furthermore a number of explorative analyses will be performed on the effects of the two modalities on the explorative outcomes (gait, walking performance and the family-centred behaviour of health care providers).

**Consensus of recommendations**

*Reviewer 3, comment 11:* Page 8, line 193: remove the last sentence. It is highly unlikely that there will not be consensus, and it would be inappropriate to conduct an examination like IGA without providing a report and treatment options (if not a single recommendation)

*Author’s reply:* The sentence about consensus is related to each of the interventions that might be recommended. In order to clarify this, the following changes have been made to the manuscript.

*Revised text, page 9, line 198-199:* Finally, each of the recommendation for interdisciplinary interventions will be based upon consensus. Otherwise, the specific intervention will not be recommended.

**Language changes**

*Reviewer 3, comment 12 (page 13, line 308):* change ‘two intervention arms’ to ‘experimental and control groups’

*Author’s reply:* The text has been revised as suggested.

*Revised text, page x, line xx:* Any adverse events that occur in the experimental and control groups will be registered…
Sample size

Reviewer 3, comment 13 (page 13): Sample size: why not use the Gait Profile score and then calculate your sample size based on the published MCID for this?

Author’s reply: For sensitivity reasons as also stated earlier we have chosen GDI as primary outcome, therefore the sample size calculation should be based on minimal clinical important differences (MCID) specified for GDI. However when comparing our 7.9 point to the proposed 1.6° with GPS, which is equal to half the distance between two GMFCS levels on 2.9°, we do believe our estimate is comparable, as the differences in GDI between GMFCS levels on our sample is 14 point, corresponding to a MCID on 7 point [14]. Furthermore different methods to determine MCID have been proposed. It is widely accepted that a patient-centred approach to determine the MCID is the anchor based method. This work has not been done for GDI, which allow us to believe that our method is acceptable.
References


