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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

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Supplementary Appendix

Specialist physiotherapy for functional motor disorder (Physio4FMD): a pragmatic, multicentre randomised controlled trial

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1. Protocol Revision History

Version number	Version date	Reason for Change
1·0	17/02/2018	Final first version.
2·0	02/07/2018	Addition of Trial Manager contact details. Minor changes to exclusion criteria no. 3. Error corrected on summary page exclusion criteria. Summary page adjusted to reflect inclusion from inpatients as well as outpatients. Addition of Extended PHQ outcome measure. Addition of Confidence in correctness of diagnosis of FMD outcome measure. Changes to the wording of the SAE reporting section.
3·0	15/03/2019	Amending reference to all participants requiring at least 24 hours to consider the PIS before consent. Changing the screening period from 28 days to 8 weeks. Amending the start and end months of the internal pilot phase.
4·0	11/02/2020	Updating the sponsor representative. Addition of Prof Irwin Nazareth as a collaborator. Other minor changes to collaborator job titles and contact details. Updating the sample size calculation to reflect up to 30% drop out. Adding text message and email contact to allow follow up of missing follow up outcome measures. Correcting the error WPAI-GH to WPAI-SHP in section 16. Some minor grammatical corrections.
5·0	28/10/2020	Addition of COVID-19 risk assessment and management strategy statement.
6·0	09/02/2021	Addition of a qualitative interview with trial physiotherapists.
7·0	11/05/2021	Updating the sponsor representative. Updating the trial flow chart figures. Amending the COVID-19 risk statements to include additional measures for recruitment. Changing the end of trial date and funding statement. Updating the sample size with additional recruitment. Updating the statistical and health economic analysis section with COVID-19 impact plan.

2. The neurologists' guide to eligibility, explaining the diagnosis and introducing the trial

Eligibility Criteria

Inclusion criteria

1. New or returning patients presenting to participating outpatient neurology clinics and neurology inpatients.
2. The patient has a "clinically definite" diagnosis of FMD according to the Gupta and Lang classification criteria.[a]
3. Age 18 or over.
4. Diagnostic investigations have come to an end.
5. The patient is accepting of the intervention.
6. Motor symptoms must be sufficient to cause significant distress or impairment in social, occupational or other important areas of functioning (subjectively described by the patient), independent of other comorbidities.

Exclusion criteria

1. The recruiting neurologist deems the patient to have severe psychiatric comorbidity, including factitious disorder, self-harm, anxiety and depression, which would interfere with the patient's ability to participate in physiotherapy.[b]
2. The patient has an organic diagnosis which explains the majority of their symptoms or disability.
3. The patient has pain, fatigue or dissociative seizures that would interfere with their ability to engage in the trial physiotherapy intervention.
4. Disability to the extent that the patient requires assistance for toileting.
5. The patient is unable to attend 9 sessions of physiotherapy over a 3 week period, within 6 weeks of initial neurology consultation.
6. Ongoing unresolved compensation claim or litigation.
7. The patient has no fixed address or is seeking rehousing through their council for disability access reasons.
8. Unable to understand English sufficiently to complete questionnaires.
9. The patient has a documented learning disability that prevents them from answering questionnaires independently.
10. The patient lacks capacity to give consent.

[a] Gupta and Lang "Clinically Definite" diagnosis requires the following criteria to be met
Remittance with suggestion, physiotherapy, psychotherapy, placebos or while the patient is unobserved.
Inconsistent over time / incongruent with clinical condition
Other manifestations: other 'false' signs, multiple somatizations, obvious psychiatric disturbance
Gupta A, Lang AE. Psychogenic movement disorders. *Curr Opin Neurol* 2009;**22**:430–6. doi:10.1097/WCO.0b013e32832dc169

[b] The decision to exclude a patient due to psychiatric comorbidity is a clinical decision made by the neurologist, rather than a decision based on a screening tool or questionnaire. We believe that no single screening tool or questionnaire would serve this purpose. Additionally, there is insufficient data on which to base cut-off scores to exclude patients on any particular questionnaire.

Interpreting the eligibility criteria

It is important to exclude patients who are not suitable for the intervention. The main categories of exclusion that we are concerned about are:

- Persistent and severe pain: Chronic pain occurs in most patients with FND. We are not excluding patients with chronic pain, but we are concerned when chronic pain is exacerbated so much by

even minimal physio that it makes progress very difficult. Some markers of this might be pain that can take many hours before it returns to normal levels after exacerbation or pain that reaches 10/10 with minimal physical activity.

- Chronic fatigue: It's a similar issue with fatigue. Most patients will feel tired after physio sessions and may need to rest after. It's a question of whether fatigue is going to be a rate-limiting step, for example, the patient needs to rest for several days and can't engage in any of the tasks related to their physiotherapy as a consequence.

- The intervention involves 9 sessions, which need to be completed within 3 weeks. This means the patient will need to be able to tolerate 2 sessions in one day, separated by a lunch break. The sessions involve blocks of activity (e.g. sit to stand, walking on a treadmill) separated by rests. If the patient's level of pain of fatigue prevents them from doing this they are unsuitable for the intervention.

- Psychiatric or psychological comorbidity: Again, judgement is required. We do not need to exclude patients because of anxiety or depression or psychological comorbidity per se, but when it is clear that these factors are an obstacle to physical therapy they should be excluded. Particular red flags are: Recent active and serious self-harm (minor self-harm, especially if longstanding may not be a barrier to treatment); and, personality disorder leading to conflict with multiple health professionals.

Explaining the diagnosis to patients

Some degree of standardisation is necessary for the trial. Important ingredients of the explanation are as follows, although we encourage the use of individualised 'recipes' from these ingredients depending on the patient's circumstances and prior views.

1. **Give it a name:** "You have functional… (weakness/tremor/neurological disorder/motor disorder)" (we are generally not prescriptive about terminology but in this trial Physio4FMD we think it would be better if everyone standardises around that terminology).
2. **Explain what this means:** This means that there is problem with abnormal nervous system functioning which affects your ability to control your movement +/- perceive normal sensations.
3. **Explain how you made the diagnosis** – demonstrate or explain Hoover's sign, tremor entrainment, variability of symptoms, etc.
4. **Explain that it is real and common:** "FND is a common condition that we see regularly in neurology. It is a real condition, and I don't think that you are making it up or that it is "all in your head".
5. **Explain what this does not mean**: It is not caused by a structural problem or damage to your nervous system.
6. **Discuss How vs Why:** How – attention interferes with movement. Why – this is a difficult question to answer, multifactorial, risk factors can be physical and psychological. But there is still a lot we do not know, which is no different from most other neurological conditions, such as MS or Parkinson's disease.
7. **Discuss relevant comorbidity:** e.g. "I think you have migraine, and this might be making your movement problem worse. We need to treat your migraine, which will help.
8. **Discuss treatment options:** "There are different treatment options available, although sometimes they can be hard to access. As your problem affects your movement, physiotherapy can be helpful. For some people psychological treatment can be helpful. If things get worse, it is possible to be referred to inpatient treatment… I think we should start with physiotherapy.
9. **Discuss the trial**

Trial participants are not excluded from receiving other treatment and therapy. It may be appropriate to arrange for them to also see an occupational therapist. If you feel they would benefit from seeing a psychologist/CBT therapist, it may be worth considering if they meet the eligibility criteria.

Discussing the Trial with Patients

How you introduce and discuss the trial to prospective participants is important. In particular, it is important that you describe the trial interventions from a position of equipoise to avoid biasing the trial. Patients may immediately presume the study intervention is likely to be better than the control (treatment as usual). This is a limitation of non-blinded trials, however we should do our best not to add to this perception.

If the patient perceives the intervention to be significantly better than the control:

- This may have a nocebo effect on the control group results, which will bias the trial.
- Participants disappointed to be in the control group are more likely to drop out, which may lead to insufficient statistical power at the end of the trial.

How to introduce the trial

- Physiotherapy seems to be helpful for many people with FMD, however nobody has done a large clinical trial to prove this.
- It is important to have evidence form a clinical trial to convince the NHS to make physiotherapy more available for people with FMD.
- We are running a trial comparing two different types of physiotherapy, you may be interested in taking part.
- In the trial you will be randomised to receive one of two different types of physiotherapy, its 50:50 chance which type you will receive.
- One type is normal neuro-physiotherapy – you will be referred to your local service. The other type is a particular physiotherapy programme that is completed a bit more intensively over 3 weeks here at this hospital.
- Unfortunately, you can't choose which group you get, but we think both are likely to be helpful. The trial will test if one is better than the other.
- Here is an information sheet about the trial which you can read in your own time.
- Can I ask one of my colleagues to get in touch with you to give you more information?

Things to avoid saying

- The trial physiotherapy is a special physio for your condition FMD.
- The trial physiotherapy was much more effective than neuro-physiotherapy in the first pilot trial.
- If you don't get the special physio in the trial, then we can make sure you get it at the end anyway.
- Getting into details about the pros and cons of each treatment (e.g. one type of physiotherapy might be better because its more intensive, or worse because intensive treatment is tough. Keep it simple).

Can you offer control group participants the trial intervention after they have left the trial?

- If it appears that the study intervention is effective and your patient does not benefit from control physiotherapy, we encourage you to try to arrange for control participants to access treatment from the intervention physios.
- However, it is important that you do not promise this from the beginning as this will add to the perception that they are not getting effective treatment, which is likely to have a nocebo effect.
- You can discuss this with the patient by saying, "If you do not improve with physiotherapy, there are other treatment options available and we can consider these in your follow up visit. Improvement from FMD is often slow, so we need to wait and see.

Patient Follow-up

The trial protocol requires the neurologist to provide at least one follow up visit within 12 months of their initial consultation. There is no requirement as to how many times or when this occurs as long as it happens once. Follow up should ideally be from the same neurologist, or a neurologist supervised by the same neurologist.

The follow up visit is an opportunity to see how the patient has fared with their intervention allocation. As you will not be blinded, you may get a sense of whether the different trial conditions are helpful. It is important that you do not bias the trial by discussing your perception of the interventions prior to the patient's completion of the trial (12 months from the date they signed up).

If the patient has seen little improvement, it may be appropriate to refer on to further treatment. For example, psychiatry assessment, clinical Psychology, or multidisciplinary rehabilitation. It is ok to make the above referrals while the patient is still involved in the trial.

If the patient was in the control group and the intervention physiotherapist has the capacity to see more patients, you can refer the patient. <u>This treatment should not start until after they have completed their 12-month data and left the trial</u>.

Suggested text to be included in referral letter to treatment as usual

"Mr/Ms XXX has consented to participate in an NIHR funded RCT investigating treatment for FND. He/She has been allocated to the control group, which is 'treatment as usual'. Please treat according to your normal practice and local procedures."

Add a link to the NIHR page for the trial and invite the physiotherapist to contact the trial lead (Glenn Nielsen) if they would like more information. Physiotherapists requesting information about treatment of FMD will be directed to published consensus recommendations for physiotherapy treatment of FMD.[1]

3. Participant Information Sheet and Consent Form

INSERT LOCAL NHS TRUST HEADER HERE

PARTICIPANT INFORMATION SHEET
Version 4.0, 11/05/2021

A Randomised Controlled Trial of Specialist Physiotherapy for Functional Motor Disorder (Physio4FMD)

We are inviting you to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Please ask us if there is anything that is not clear or if you would like more information. Take your time to decide whether or not you wish to take part.

Thank you for taking the time to read this information sheet

What is the purpose of the study?
Physiotherapy is often recommended for people with functional motor disorder (symptoms such as weakness, tremor or muscle spasms where there is no damage to the nervous system) but there is little scientific evidence to show whether or not it is helpful.

In this study, we will compare two types of physiotherapy to see if one is more effective than the other for people with functional motor disorder.

Do I have to take part?
No. It is up to you to decide whether or not to take part and you are free to withdraw at any time. If you decide to take part we will ask you to sign a consent form indicating your willingness to participate in the study. A decision to withdraw, or a decision not to take part, will not affect the standard of care you receive. If you choose not to take part or to withdraw from this study your neurologist can refer you to your local physiotherapy service.

If you withdraw from the study, we will continue to use any information we have collected about you, unless you ask us not to.

What will I have to do if I take part?
If you choose to take part you will be asked to complete a questionnaire booklet to give us more information about your health – we can help you complete this if need be. This will take between 30 and 60 minutes in total.

The information you provide will remain strictly confidential, will be stored securely and will only be seen by the research team.

Treatment groups
You will then be allocated by chance to one of two treatment groups.

Group 1
Participants in this group will be referred to their local physiotherapy service for standard physiotherapy treatment. If you are currently receiving physiotherapy or have recently been discharged, a letter summarising your consultation with your neurologist will be sent to your local physiotherapy team. You will receive a copy of this letter.

Group 2
Participants in this group will receive the research physiotherapy programme at a physiotherapy department near where you saw your neurologist. The physiotherapy will involve between 6 and 9 physiotherapy sessions, which will be scheduled over three weeks. The physiotherapist will then follow you up after three months, in person or over the telephone, to see how you are going.

Both Groups
We will ask you to complete the questionnaire booklet again six months after you have signed up to the study and again after 12 months. Repeat questionnaire booklets will be sent to you by post with a return-paid envelope. You will also be given the option of completing the questionnaires by telephone, or a secure online (internet) form. We will remind you by telephone or email if you forget to fill in the booklet.

You will also be contacted by telephone after you have completed your physiotherapy treatment. We will ask you to describe the treatment you received and rate your satisfaction with this treatment. We will not share this information with your physiotherapist.

How do you decide which group I am in?
You will be assigned to one of the two groups by chance.

At the moment we do not know if one type of physiotherapy is better than another. We will compare two different physiotherapy approaches by selecting the group you are assigned to by chance, using a computer programme. You will have a 50:50 chance of being in either group.

How long will I be in the study?
If you agree to take part you will be in the study for 12 months. After this you will return to standard NHS care.

We will also ask for your permission to contact you to find out about your health after you complete the study. We would like to find out how your health changes after two years, five years and ten years. You may choose to opt out of this part of the study. Also, at any time you may ask for your contact details to be removed from this list and you will no longer be contacted.

Expenses and Payments
We will reimburse your travel costs to your physiotherapy appointments up to the value of £25 per visit.

What are the benefits of taking part?
We cannot promise that the study will help you, but the information from this study may help improve future physiotherapy treatment of functional motor disorder. We also hope to increase awareness of functional motor disorders amongst physiotherapists and other health care professionals.

What are the possible risks?
Physiotherapy is considered a standard and safe treatment for people with functional motor disorder. We believe there are no additional risks in taking part in this research study.

What about COVID-19?
As you are likely aware, due to the outbreak of COVID-19 (Coronavirus), NHS Trusts are taking extra steps to ensure both staff and patients are kept safe at all times and to prevent any further spread.

As part of this you will be asked to follow our Hospital policies on social distancing and Personal and Protective Equipment (PPE) whilst you attend on-site.

Staff will be adhering to strict cleanliness guidelines and, in some cases, this may mean wearing PPE, such as a face mask, a plastic gown and/or gloves.

You may bring a support person or carer to appointments if you need to, but where possible, please attend on your own.

Please don't attend hospital if you:

1) Are under current instruction from your doctor that you should be isolating and avoiding social contact.
2) Have a household member, or are yourself, currently experiencing any COVID-19 symptoms, in which case you must stay at home and please contact us so we can postpone any appointments.

Depending on the hospital policy at the time of your appointment, you may be contacted by a member of the research or treatment team prior to appointments to check for COVID-19 symptoms.

If you do not feel comfortable attending the hospital for treatment due to COVID-19, you are under no obligation to participate in the research. If this is the case or you have any additional concerns or questions regarding COVID-19, please use the contact details of the local hospital team, provided in the following section of this Information Sheet.

What if there is a problem?
We do not anticipate anybody to come to any harm by taking part in this study. If you have a concern about any aspect of this study, you should ask to speak to the person in charge of this study at your hospital/neurology department. Their contact details are …

If you remain unhappy and wish to complain formally, you can do this via the NHS Complaints Procedure. The Patient Advice and Liaison Service (PALS) can support you through this process. Contact PALS via your hospital switchboard.

Will my taking part be kept confidential?
Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. You will be allocated a unique study code in order to keep any information stored about you confidential. All research staff not directly involved with you will only know you by this code. Information will be stored on a secure password protected computer database and will only be accessible to the research team and potentially by regulatory authorities for auditing and monitoring purposes. When the results of the study are reported, individuals who will have taken part will not be identified in any way.

St Georges, University of London is the sponsor for this study based in the United Kingdom. We will be using information from you and/or your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. St Georges, University of London may keep information collected for the purpose of the study up to 10 years after the study has finished. This is to ensure integrity of the results. All data will be stored in a secure manner.

[SITE NAME] will collect information from you and/or your medical records for this research study in accordance with our instructions.

[SITE NAME] will use your name, contact details and other identifiers to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from St Georges, University of London, (SITE NAME) and regulatory organisations may look at your medical and research records to check the accuracy of the research study. [SITE NAME] will pass these details to St Georges, University of London along with the information collected from you and/or your medical records. The only people in St Georges, University of London who will have access to information that identifies you will be people who need to contact you to as part of the research study you are involved in, and or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name or contact details.

[SITE NAME] will keep identifiable information about you from this study for 10 years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage the data in specific ways to ensure the research we conduct is reliable and accurate. If you withdraw your consent to participate in a research project, this will not mean we will have to remove all data as well. We will keep the information about you that we have already obtained to ensure research integrity is maintained in the public's interest. To safeguard your rights, we will strive to use the minimum personally-identifiable information possible.

You can find out more about how we use your information https://www.stgeorges.nhs.uk/education-and-research/research/research-privacy-notice/

For general information on how the NHS uses research data please visit https://www.hra.nhs.uk/information-about-patients/

Will my GP be informed about my participation?
Yes, we will send a letter to your GP informing them of your participation. Any medical or physiotherapy letters or reports from the study will be copied to you and your GP.

How will the information be used?
The findings of this research will be published in scientific journals and presented at conferences. You will be informed about the results by the researchers, who will provide you with a study newsletter informing you of the progress of the trial and a plain English summary of the results when the trial is completed. We will also let you know how to access the scientific publications.

The plain English summary will also be sent to online patient support organisations, such as www.FNDHope.org and www.FNDAction.org.

Who is funding this research?
Funding for this research is provided by the National Institute for Health Research (NIHR).

Who has reviewed this study?
This study has been reviewed and approved by the National Institute for Health Research (NIHR) and the Health Research Authority (HRA).

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and approved by the London – Surrey Borders Research Ethics Committee.

Contact details
If you have any questions or concerns, please contact –
The Trial Manager, Hayley Noble
Tel: 020 8266 6468
Email: hnoble@sgul.ac.uk

For further information, please visit our website: www.Physio4FMD.org

This research project is registered on the following database –
ISRCTN registry [https://www.isrctn.com/ISRCTN56136713
Registration Number: ISRCTN56136713

INSERT LOCAL NHS TRUST HEADER HERE

CONSENT FORM

Centre Number:

Study Number: 17.0258

ISRCTN Registry Number: ISRCTN56136713

Participant Identification Number for this trial:

Title of Project: **A Randomised Controlled Trial of Specialist Physiotherapy for Functional Motor Disorder (Physio4FMD)**

	Please initial box
1. I confirm that I have read the information sheet dated 11.05.2021 (Version 4.0) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.	☐
3. I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from St George's University of London, relevant regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	☐
4. I understand that the information collected about me will be used to support other research in the future, and may be shared anonymously with other researchers.	☐
5. I agree to my General Practitioner being informed about my participation in the study.	☐

6. I understand that the information held and maintained by NHS Digital / NHS Scotland about me will be used to provide information about the number of hospital appointments I have had during the study period. ☐

7. I give my consent to be contacted by the study team after I have completed the study to answer questions about my health. The study team would like to find out how study participants' health changes after two years, five years and ten years. I understand that at anytime I can ask for my contact details to be removed from this list and I will no longer be contacted. ☐

8. I agree to take part in the above study. ☐

_____	_____	_____
Name of Participant	Date	Signature
_____	_____	_____
Name of Person taking consent	Date	Signature

When completed: 1 for participant; 1 for researcher site file; 1 (original) to be kept in medical notes.

4. The Specialist Physiotherapy Training Programme and Supervision

The trainers	The trainers were Glenn Nielsen, Kate Holt, and Cameron Moss. They are physiotherapists who have specialised in neurology and neurorehabilitation, and they had two or more years of experience of delivering the trial intervention protocol.
Duration of training	Five consecutive days, Monday to Friday.
Content	<u>Background Reading</u> The trial physiotherapists were asked to read the following papers as the minimum background reading, prior to attending. • Espay, A. J., Aybek, S., Carson, et al. (2018). Current concepts in diagnosis and treatment of functional neurological disorders. *JAMA Neurology*, *75*(9), 1132–1141. https://doi.org/10.1001/jamaneurol.2018.1264. • Nielsen, G., Stone, J., Matthews, et al. (2015). Physiotherapy for functional motor disorders: a consensus recommendation. *Journal of Neurology, Neurosurgery & Psychiatry*, *86*(10), 1113–1119. https://doi.org/10.1136/jnnp-2014-309255 • Stone, J. (2009). The bare essentials: Functional symptoms in neurology. *Pract Neurol*, *9*(3), 179–189. https://doi.org/10.1136/jnnp.2009.177204 <u>Observation and Participation in Treatment</u> Over the five days, each physiotherapist observed and participated in treating two patients. For each patient, the treatment was led by a different trainer. The 9 sessions of the intervention protocol were scheduled over the 5 days, with two sessions a day separated by break, e.g.: • Patient A, session 1: 9:00 – 10:00; session 2: 13:00 – 14:00 (Trainer X) • Patient B, session 1: 10:30 – 11:30; session 2: 14:30 – 15:30 (Trainer Y) <u>Clinical and Theoretical Discussions</u> Each afternoon, after completing the treatment sessions, the physiotherapist and the trainers discussed each component of the intervention completed on that day, with reference to the intervention protocol, the theoretical underpinnings of the intervention, and how treatment might be adapted for other patient presentations.
Assessment of competence	Competency was assessed according to a checklist that ensured each physiotherapist had demonstrated an understanding of delivering the key ingredients of the treatment protocol.
Training manual	The training was supplemented by a treatment manual, which is available to download.[2]
Supervision	For each participant treated in the specialist physiotherapy group, the physiotherapist completed a supervision session with one of the trainers. The supervision session was conducted over telephone, and lasted up to 30 minutes. The following topics were discussed during supervision: (i) the onset of the participant's symptoms; (ii) the main problems related to physiotherapy; (iii) how the symptom model could be used to help the patient understand their symptoms; (iv) a planned treatment progression; and (v) potential barriers to engaging in physiotherapy. Supervision aimed to provide clinical support and improve fidelity to the intervention protocol.

5. Secondary outcome measure: Clinical Global Impression Scale of Change

Clinical Global Impression Scale (CGI-I)

After physiotherapy, the problem with my movement is:
(please tick one box)

✓ Please tick one box

☐	Much improved
☐	Improved
☐	No change
☐	Worse
☐	Much worse

Thank you

6. Secondary outcome measure: Fatigue 5-point scale

Fatigue

Which best describes your level of fatigue or tiredness TODAY

I have no tiredness or fatigue	❑
I have slight tiredness or fatigue	❑
I have moderate tiredness or fatigue	❑
I have severe tiredness or fatigue	❑
I have extreme tiredness or fatigue	❑

Thank you

7. Secondary outcome measure: Confidence in the diagnosis

Confidence in the diagnosis

How strongly do you believe that you have been given the correct diagnosis of functional motor disorder?

(Please circle a number between 0 and 10)

0 … Not at all confident

1

2

3

4

5 … Somewhat confident

6

7

8

9

10 … Extremely confident

Thank you

8. Extended Patient Health Questionnaire (PHQ-15 Extended)[3,4]

During the past month have you been bothered a lot by…?

1	Paralysis or weakness of an arm or leg	☐ Yes	☐ No	
2	Double or blurred vision	☐ Yes	☐ No	
3	Difficulty swallowing or a lump in the throat	☐ Yes	☐ No	
4	Difficulty speaking or slurred speech	☐ Yes	☐ No	
5	Stomach pain	☐ Yes	☐ No	
6	Back pain	☐ Yes	☐ No	
7	Pain in your arms, legs or joints (knees, hips, etc)	☐ Yes	☐ No	
8	For women: menstrual pain or problems	☐ Yes	☐ No	☐ Not applicable
9	Pain or problems during intercourse	☐ Yes	☐ No	
10	Headaches	☐ Yes	☐ No	
11	Chest pain	☐ Yes	☐ No	
12	Dizziness	☐ Yes	☐ No	
13	Fainting spells	☐ Yes	☐ No	
14	Feeling you heart pound or race	☐ Yes	☐ No	
15	Loss of sensation, numbness or tingling	☐ Yes	☐ No	
16	Problems with your memory or concentration	☐ Yes	☐ No	
17	Partial or total loss of vision	☐ Yes	☐ No	
18	Partial or total loss of hearing	☐ Yes	☐ No	
19	Shortness of breath	☐ Yes	☐ No	
20	Constipation, loose bowels or diarrhoea	☐ Yes	☐ No	
21	Nausea, gas or indigestion	☐ Yes	☐ No	
22	Feeling tired or having low energy	☐ Yes	☐ No	
23	Trouble sleeping	☐ Yes	☐ No	
24	Little interest or pleasure in doing things	☐ Yes	☐ No	
25	Feeling down, depressed or hopeless	☐ Yes	☐ No	
26	“Nerves” or feeling anxious or on edge	☐ Yes	☐ No	
27	Worrying about a lot of different things	☐ Yes	☐ No	
28	Lack of co-ordination or balance	☐ Yes	☐ No	
29	A seizure or fit	☐ Yes	☐ No	
30	An anxiety attack (suddenly feeling fear or panic)	☐ Yes	☐ No	
31	Problems or difficulty urinating (passing water)	☐ Yes	☐ No	

Thank you

9. COVID-19 impact on the trial, mitigation strategy, and sensitivity analyses

Timeline

11 February 2020: Prior to the pandemic, a decision was made to increase the recruitment target to allow for a potential greater than anticipated loss to loss to follow-up. The original target was 264, the new target was 300. The decision was influenced by a healthy recruitment rate, and we were likely to achieve our prior target before the end of the designated recruitment period. The amendment was approved by the research ethics committee on 11 February 2020.

23 March 2020: The first national COVID-19 lockdown was instigated. As part of the COVID-19 pandemic response, non-essential NHS services and face-to-face research activity was suspended. All Physio4FMD face-to-face activity had been put on hold by 23 March 2020. At this time the total recruitment was 267, and there were 89 participants waiting to receive their trial-allocated treatment. Amongst those whose treatment was interrupted due to COVID-19, there were 27 allocated to specialist physiotherapy and 62 allocated to treatment as usual. The difference in distribution can be accounted for by the longer wait to receive treatment as usual compared to specialist physiotherapy. The suspension of face-to-face treatment was lifted at different times for each of the 11 sites, depending on local policies and regional variations in the pandemic response. Most sites were given permission to restart after six to nine months. Only 30 of the 89 (33.7%) participants whose treatment was interrupted went on to receive their allocated physiotherapy within the 12-month follow-up period. Six- and 12-month follow-up assessments continued during the pandemic response, regardless of whether participants received treatment.

3 August 2021: An extension to the trial was granted and recruitment recommenced. From the period of 3 August 2021 to 28 January 2022, an additional 88 participants were recruited. The final 12-month follow-up was completed 28 January 2023.

COVID-19 mitigation strategy and analysis plans

The mitigation strategy and analysis plans were determined and published prior to database lock.[5] Participants were categorised according to where they were in their trial journey at the time that national lockdown was enforced on 23 March 2020. See also figure below.

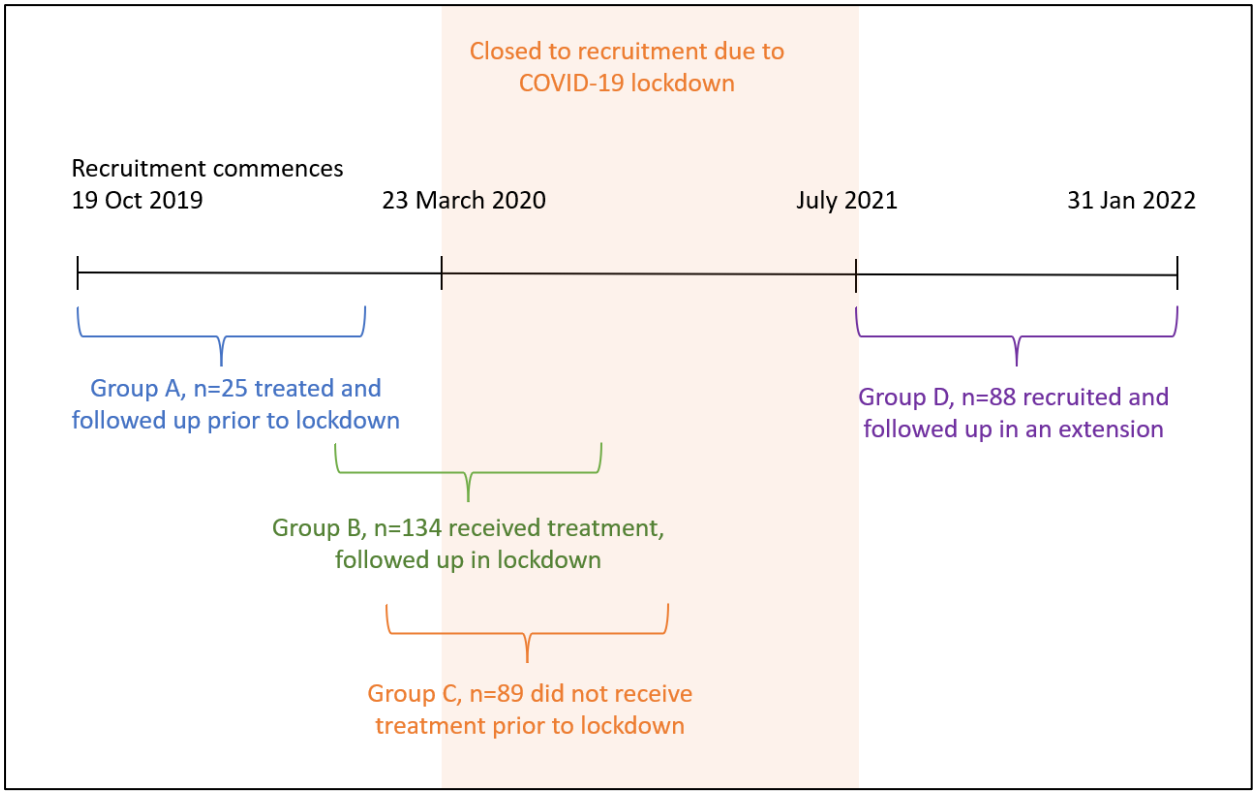
Group A: (n=25) Randomised, received treatment, and completed follow-up prior 23 March 2020.

Group B: (n=134) Randomised, received treatment prior to 23 March 2020, completed 12-month follow up after 23 March 2020.

Group C: (n=89) Randomised prior to 23 March 2020, did not receive treatment prior to lockdown, completed 12-month follow-up after 23 March 2020.

Group D: (n=88) Randomised, completed treatment and 12-month follow-up in the extension (after 23 March 2020).

19 participants were unaccounted for in these groups as they were uncontactable at the time and their treatment status could not be determined.



Supplementary Figure 9.1 Recruitment and follow-up time lines in relation to the COVID-19 pandemic.

Most of the participants in group C did not receive their trial allocated treatment during the 12-month follow up period (66·3%). For those who received treatment, it was substantially delayed and received close to the 12-month assessment. We therefore treated data from participants in group C as missing and they were excluded from the primary analysis. We conducted three sensitivity analyses; (i) to explore the impact of excluding COVID group C from the primary analysis, we repeated the analysis including all randomised participants with a fixed effect for lack of treatment due to the pandemic; (ii) to explore whether treatment effect differs following the pandemic, we compared COVID groups A and B to group D; and (iii) to determine if attending more sessions affected outcome, we conducted a dose response analysis.

10. Baseline characteristics table for Group C

Supplementary table 10.1. Baseline Characteristics of Group C (participants recruited prior to 23 March 2020 and did not receive their trial allocated treatment prior to the first COVID-19 lockdown on 23 March 2020) and those unallocated to a COVID group due to withdrawal or they were unable to be contacted.

	Specialist Physiotherapy (n=38)	**Treatment as usual (n=70)**	**Total (n=108)**
Age, years			
Mean (SD)	45·0 (15·2)	41·2 (14·3)	42·6 (14·7)
Median (IQR)	46·5 (33 – 56)	42·6 (28 – 53)	43·5 (29 – 53·5)
Gender			
Male	15/38 (39·5%)	18/70 (25·7%)	33/108 (30·6%)
Female	23/38 (60·5%)	52/70 (74·3%)	75/108 (69·4%)
Ethnicity			
White	34/38 (89·5%)	61/70 (87·1%)	95/108 (88·0%)
Black	2/38 (5·3%)	1/70 (1·4%)	3/108 (2·8%)
Asian	1/38 (2·6%)	3/70 (4·3%)	4/108 (3·7%)
Mixed	1/38 (2·6%)	4/70 (5·7%)	5/108 (4·6%)
Other	0/38 (0·0%)	1/70 (1·4%)	1/108 (0·9%)
Relationship status and dependents			
Married or cohabitating with partner	26/38 (68·4%)	43/70 (61·4%)	69/108 (63·9%)
Single, separated, or widowed	12/38 (31·6%)	27/70 (38·6%)	39/108 (63·1%)
Has dependents	19/38 (50·0%)	43/70 (61·4%)	62/108 (57·4%)
Care needs			
Has a carer	13/38 (34·2%)	22/70 (31·4%)	35/108 (32·4%)
Has a paid carer	9/38 (23·7%)	15/70 (21·4%)	24/108 (22·2%)
Highest qualification, years of education			
No qualification	5/38 (13·2%)	1/69 (1·5%)	6/107 (5·6%)
General Certificate of Secondary Education	7/38 (18·4%)	15/69 (21·7%)	22/107 (20·6%)
A level	3/38 (7·9%)	13/69 (18·8%)	16/107 (15·0%)
National Vocational Qualification	7/38 (18·4%)	7/69 (10·1%)	14/107 (13·1%)
Higher National Certificate/Diploma	6/38 (15·8%)	11/69 (15·9%)	17/107 (15·9%)
Degree	5/38 (13·2%)	14/69 (20·3%)	19/107 (17·8%)
Higher Degree	3/38 (7·9%)	8/69 (11·6%)	11/107 (10·3%)
Other	2/38 (5·3%)	0/69 (0·0%)	2/107 (1·9%)
Years of education (SD)	13·2 (2·6)	14·5 (2·5)	14·1 (2·6)
Employment status			
Working or studying	12/38 (31·6%)	29/70 (41·4%)	41/108 (38·0%)
Not working/studying because of sickness	11/38 (29·0%)	19/70 (27·1%)	30/108 (27·8%)
Not working because unemployment	13/38 (34·2%)	19/70 (27·1%)	32/108 (29·6%)
Other	2/38 (5·3%)	3/70 (4·3%)	5/108 (4·6%)
Previous treatment			
Physiotherapy	9/34 (26·5%)	34/65 (52·3%)	43/99 (43·4%)
Psychology	2/31 (6·1%)	13/65 (20·0%)	15/96 (15·6%)
Occupational Therapy	6/34 (17·7%)	10/65 (15·4%)	16/99 (16·2%)
Specialist inpatient rehabilitation	0/34 (0·0%)	4/65 (6·2%)	4/99 (4·6%)
Symptom duration, years			
Mean (SD)	6·0 (9·4)	3·8 (4·7)	4·6 (6·8)
Median (IQR)	2·9 (1·3 – 5·2)	1·7 (0·9 – 5·3)	2·1 (1·0 – 5·3)
Dominant motor symptom			
Weakness	12/38 (31·6%)	27/70 (38·6%)	39/108 (36·1%)
Gait disturbance	7/38 (18·4%)	19/70 (27·1%)	26/108 (24·1%)

Tremor	9/38 (23·7%)	8/70 (11·4%)	17/108 (15·7%)
Mixed movement disorder	9/38 (23·7%)	9/70 (12·9%)	18/108 (16·7%)
Jerks	1/38 (2·6%)	4/70 (5·7%)	5/108 (4·6%)
Dystonia / fixed dystonia	0/38 (0·0%)	3/70 (4·3%)	3/108 (2·8%)
Body part affected, dominant hand			
Left upper limb	15/38 (39·5%)	34/70 (48·6%)	49/108 (45·4%)
Right upper limb	24/38 (63·2%)	31/70 (44·3%)	55/108 (50·9%)
Left lower limb	20/38 (52·6%)	53/70 (75·7%)	73/108 (67·6%)
Right lower limb	29/38 (76·3%)	47/70 (67·1%)	76/108 (70·4%)
Head/neck	7/38 (18·4%)	17/70 (24·3%)	24/108 (22·2%)
Trunk	5/38 (13·2%)	12/70 (17·1%)	17/108 (15·7%)
Dominant hand, right	33/38 (86·9%)	63/69 (91·3%)	96/107 (89·7%)

11. Past Medical History (self-reported), Groups A, B and D

	Specialist Physiotherapy (N=141)		Treatment as usual (N=106)	
Participants with available data	138	97.9%	100	94.3%
Cardiovascular				
Angina/heart attack (myocardial infarction)	5/138	3.6%	3/100	3.0%
Other heart condition	4/138	2.9%	11/100	11.0%
Hypertension	19/138	13.8%	14/100	14.0%
Palpitations (subjective patient report)	6/138	4.4%	8/100	8.0%
Other	7/138	5.1%	13/100	13.0%
Respiratory				
Asthma	26/138	18.8%	21/100	21.0%
Other chronic lung disease	3/138	2.2%	1/100	1.0%
Sleep apnoea	9/138	6.5%	1/100	1.0%
Other	4/138	2.9%	3/100	3.0%
Neurology				
Carpal tunnel syndrome	8/138	5.8%	4/100	4.0%
Cognitive impairment	6/138	4.4%	1/100	1.0%
Disc herniation with neurological symptoms	1/138	0.7%	2/100	2.0%
Dyslexia	7/138	5.1%	12/100	12.0%
Epilepsy	5/138	3.6%	1/100	1.0%
Essential tremor	5/138	3.6%	2/100	2.0%
Head injury (minor) / concussion	10/138	7.3%	10/100	10.0%
Idiopathic intracranial hypertension	0/138	0.0%	0/100	0.0%
Incidental findings on MRI	5/138	3.6%	7/100	7.0%
Migraine	31/138	22.5%	31/100	31.0%
Multiple Sclerosis	1/138	0.7%	1/100	1.0%
Neurological symptoms undiagnosed, likely functional	6/138	4.4%	1/100	1.0%
Parkinson's disease	0/138	0.0%	0/100	0.0%
Peripheral neuropathy	1/138	0.7%	0/100	0.0%
Stroke	5/138	3.6%	2/100	2.0%
Tinnitus	11/138	8.0%	13/100	13.0%
Vestibular disorder	3/138	2.2%	1/100	1.0%
Brain tumour +/- surgery	1/138	0.7%	3/100	3.0%
Other[1]	10/138	7.3%	12/100	12.0%
Psychiatry				
ADHD	0/139	0.0%	1/100	1.0%
Anxiety	59/138	42.8%	45/100	45.0%
Agoraphobia	4/138	2.9%	1/100	1.0%
Autism Spectrum Disorder	0/138	0.0%	3/100	3.0%
Bipolar	3/138	2.2%	1/100	1.0%
Borderline/Emotionally unstable personality disorder	2/138	1.5%	2/100	2.0%
Depression	51/138	37.0%	50/100	50.0%
Eating disorder	5/138	3.6%	5/100	5.0%
Obsessive compulsive disorder (OCD)	2/138	1.5%	4/100	4.0%
Panic disorder (panic attacks)	8/138	5.8%	9/100	9.0%
Post-traumatic stress disorder (PTSD)	12/138	8.7%	13/100	13.0%
Other[2]	9/138	6.5%	3/100	6.0%
Genitourinary				

Bladder – incontinence	25/138	18.1%	11/100	11.0%
Bladder – retention	6/138	4.4%	5/100	5.0%
Gynaecological dysfunction*	7/102	6.9%	9/76	11.9%
Gynaecological surgery*	18/102	17.7%	13/76	17.1%
Prostate disease**	1/36	2.8%	1/24	4.2%
Urinary tract infections	13/138	9.4%	11/100	11.0%
Other	8/138	5.8%	8/100	8.0%
Gastrointestinal				
Bowel – incontinence	9/138	6.5%	3/100	3.0%
GI surgery (past 10 years)	11/138	8.0%	5/100	5.0%
Irritable bowel syndrome	24/138	17.4%	17/100	17.0%
Other	16/138	11.6%	20/100	20.0%
Musculoskeletal				
Joint replacement surgery	2/138	1.5%	1/100	1.0%
Other orthopaedic surgery	12/138	8.7%	11/100	11.0%
Shoulder pain/dysfunction	16/138	11.6%	10/100	10.0%
Spinal pain (lumbar, cervical, thoracic, SIJ)	30/138	21.7%	17/100	17.0%
Spinal surgery (lumbar, cervical, thoracic, SIJ)	5/138	3.6%	3/100	3.0%
Osteoarthritis	14/138	10.1%	4/100	4.0%
Osteoporosis	1/138	0.7%	3/100	3.0%
Fracture	16/138	11.6%	11/100	11.0%
Hypermobility/Ehlers-Danlos Syndrome	9/138	6.5%	6/100	6.0%
Other	29/138	21.0%	13/100	13.0%
Endocrinology				
Diabetes	8/138	5.8%	5/100	5.0%
Hypothyroidism	4/138	2.9%	5/100	5.0%
Other	6/138	4.4%	6/100	6.0%
Other				
Fibromyalgia	18/138	13.0%	11/100	11.0%
Chronic fatigue syndrome /ME	19/138	13.8%	19/100	19.0%
Non-epileptic attacks/dissociative seizures	21/138	15.2%	19/100	19.0%
Other	7/138	5.1%	4/100	4.0%
ENT				
Dysphonia	4/138	2.9%	1/100	1.0%
Globus (feeling of lump in throat)	3/138	2.2%	4/100	4.0%
Other	12/138	8.7%	13/100	13.0%
Dermatology	24/138	17.4%	16/100	16.0%
Ophthalmology	20/138	14.5%	10/100	10.0%
Other	32/138	23.2%	28/100	28.0%

1. Other, Neurology: Autonomic dysfunction, Bell's palsy, Cerebral aneurysm (2), Cervical dystonia (2), Complex regional pain syndrome, Dyspraxia, Dystonia type unspecified (2), headache (2), Meniere's disease, Meningitis, Neuralgia (2), Neuropathy, Seizures, Spinal syrinx, Surgical shunt, Tourette's, Tremor type unspecified.

2. Other, Psychiatry: Psychotherapy for mental health problems, claustrophobia, auditory hallucinations, REM sleep disorder, psychosis, suicide attempt, childhood trauma, flashbacks following knee surgery, memory, loss, borderline personality disorder, depersonalisation disorder, body dysmorphia.

*For females within the randomisation groups.
**For males within the randomisation groups.

12. Past Medical History (self reported), Group C

	Specialist Physiotherapy (N=38)		Treatment as usual (N=70)	
Participants with available data	38/38	100%	69/70	98.6%
Cardiovascular				
Angina/heart attack (myocardial infarction)	1/38	2.6%	1/69	1.5%
Other heart condition	2/38	5.3%	1/69	1.5%
Hypertension	7/38	18.4%	5/69	7.3%
Palpitations (subjective patient report)	2/38	5.3%	5/69	7.3%
Other	2/38	5.3%	8/69	11.6%
Respiratory				
Asthma	8/38	21.1%	18/69	26.1%
Other chronic lung disease	3/38	7.9%	2/69	2.9%
Sleep apnoea	2/38	5.3%	2/69	2.9%
Other	2/38	5.3%	6/69	8.7%
Neurology				
Carpal tunnel syndrome	2/38	5.3%	1/69	1.5%
Cognitive impairment	4/38	10.5%	7/69	10.1%
Disc herniation with neurological symptoms	0/38	0.0%	0/69	0.0%
Dyslexia	0/38	0.0%	1/69	1.5%
Epilepsy	2/38	5.3%	4/69	5.8%
Essential tremor	2/38	5.3%	6/69	8.7%
Head injury (minor) / concussion	4/38	10.5%	9/69	13.0%
Idiopathic intracranial hypertension	1/38	2.6%	2/69	2.9%
Incidental findings on MRI	4/38	10.5%	3/69	4.4%
Migraine	9/38	23.7%	23/69	33.3%
Multiple Sclerosis	0/38	0.0%	0/69	0.0%
Neurological symptoms undiagnosed, likely functional	5/38	13.2%	3/69	4.4%
Parkinson's disease	1/38	2.6%	0/69	0.0%
Peripheral neuropathy	0/38	0.0%	3/69	4.4%
Stroke	1/38	2.6%	3/69	4.4%
Tinnitus	3/38	7.9%	6/69	8.7%
Vestibular disorder	0/38	0.0%	0/69	0.0%
Brain tumour +/- surgery	2/38	5.3%	2/69	2.9%
Other[1]	3/38	7.9%	10/69	14.5%
Psychiatry				
ADHD	0/38	0.0%	0/69	0.0%
Anxiety	21/38	55.3%	36/69	52.2%
Agoraphobia	1/38	2.6%	3/69	4.4%
Autism Spectrum Disorder	0/38	0.0%	2/69	2.9%
Bipolar	0/38	0.0%	1/69	1.5%
Borderline/Emotionally unstable personality disorder	1/38	2.6%	3/69	4.4%
Depression	22/38	57.9%	31/69	44.9%
Eating disorder	0/38	0.0%	1/69	1.5%
Obsessive compulsive disorder (OCD)	2/38	5.3%	2/69	2.9%
Panic disorder (panic attacks)	7/38	18.4%	5/69	7.3%
Post-traumatic stress disorder (PTSD)	3/38	7.9%	6/69	8.7%
Other[2]	1/38	2.6%	0/69	0.0%
Genitourinary				

Bladder – incontinence	7/38	18.4%	7/69	10.1%
Bladder – retention	4/38	10.5%	7/69	10.1%
Gynaecological dysfunction*	1/23	4.4%	2/52	3.9%
Gynaecological surgery*	5/23	21.7%	5/52	9.6%
Prostate disease**	0/15	0.0%	0/17	0.0%
Urinary tract infections	5/38	13.2%	9/69	13.0%
Other	2/38	5.3%	9/69	13.0%
Gastrointestinal				
Bowel – incontinence	3/38	7.9%	3/69	4.4%
GI surgery (past 10 years)	0/38	0.0%	2/69	2.9%
Irritable bowel syndrome	6/38	15.8%	17/69	24.6%
Other	9/38	23.7%	6/69	8.7%
Musculoskeletal				
Joint replacement surgery	2/38	5.3%	1/69	1.5%
Other orthopaedic surgery	2/38	5.3%	3/69	4.4%
Shoulder pain/dysfunction	3/38	7.9%	9/69	13.0%
Spinal pain (lumbar, cervical, thoracic, SIJ)	9/38	23.7%	12/69	17.4%
Spinal surgery (lumbar, cervical, thoracic, SIJ)	4/38	10.5%	7/69	10.1%
Osteoarthritis	7/38	18.4%	11/69	15.9%
Osteoporosis	1/38	2.6%	3/69	4.4%
Fracture	10/38	26.3%	11/69	15.9%
Hypermobility/Ehlers-Danlos Syndrome	3/38	7.9%	12/69	17.4%
Other	5/38	13.2%	13/69	18.8%
Endocrinology				
Diabetes	2/38	5.3%	4/69	5.8%
Hypothyroidism	2/38	5.3%	2/69	2.9%
Other	4/38	10.5%	3/69	4.4%
Other				
Fibromyalgia	3/38	7.9%	9/69	13.0%
Chronic fatigue syndrome /ME	5/38	13.2%	8/69	11.6%
Non-epileptic attacks/dissociative seizures	6/38	15.8%	12/69	17.4%
Other	4/38	10.5%	8/69	11.6%
ENT				
Dysphonia	0/38	0.0%	1/69	1.5%
Globus (feeling of lump in throat)	2/38	5.3%	3/69	4.4%
Other	2/38	5.3%	6/69	8.7%
Dermatology	7/38	18.4%	17/69	24.6%
Ophthalmology	5/38	13.2%	15/69	21.7%
Other	15/38	39.5%	18/69	26.1%

1. Other, Neurology: Hydrocephalus +/- shunt (3), Bell's Palsy (2), Cerebral aneurysm and coil, Seizure, Dyspraxia (2), Deafness, Cervical dystonia, Vertigo, Restless leg syndrome, Cervical radiculopathy.
2. Other, Psychiatry: Sleep disorder unspecified.
*For females within the randomisation groups.
**For males within the randomisation groups.

13. Waiting time and duration of treatment

Supplementary table 13.1

	Specialist Physiotherapy		Treatment As Usual	
	Group C (n=27)	**Groups A,B,D (n=141)**	**Group C (n=62)**	**Groups A,B,D (n=106)**
Number with available data	27 (100%)	140 (99·3%)	60 (96·8%)	93 (87·7%)
Number who received physiotherapy (%)	8/27 (26·6%)	132/140 (94·3%)	22/60 (36·7%)	78/93 (83·9%)
Days between randomisation and treatment starting				
Number with available data (%)	8/8 (100%)	132/132 (100%)	20/22 (90·9%)	66/78 (84·6%)
Mean (SD)	233·1 (83·5)	46·1 (35·3)	194·0 (111·4)	118·7 (77·1)
Median	253	36	174·5	97
Interquartile range	232·25 – 272·75	24·75 – 57·75	89·25 – 309·25	60·2 – 176·2
Min	40	3	24	12
Max	315	166	362	275
Days between treatment ending and completing primary outcome				
Number with available data (%)	8/8 (100%)	131/132 (99·3%)	21/22 (95·4%)	67/78 (85·9%)
Mean (SD)	117·5 (86·7)	294·0 (55·6)	88·8 (119·9)	176·8 (80·0)
Median	108	310	5	179
Interquartile range	70 – 115·75	281·5 – 323	0 – 237	123 – 237·5
Min	32	0	0	3
Max	319	349	287	350
Days between starting and completing treatment (duration)				
Number with available data (%)	8/8 (100%)	131/132 (99·3%)	21/22 (95·4%)	67/78 (85·9%)
Mean (SD)	15·4 (11·1)	26·3 (49·5)	101·9 (115·1)	101·2 (75·7)
Median	12·5	15	46	93
Interquartile range	6·5 – 20·75	10 – 21·5	15 – 179	47 – 148·5
Min	5	4	1	1
Max	36	380	380	366

14. Characteristics of the physiotherapists delivering the specialist physiotherapy

Supplementary table 14.1

Demographics, n=18		
Age as of 2019, mean (SD)	39·64 (7·45)	
Female, n (%)	12 (66·7%)	
Male, n (%)	6 (33·3%)	
Work Setting		
Outpatients	9 (50·0%)	
Inpatient, acute	2 (11·1%)	
Inpatient, rehabilitation	1 (5·6%)	
Combination	6 (33·3%)	
Highest Qualification in Physiotherapy		
Degree	10 (55·6%)	
Post Grad Diploma	2 (11·1%)	
Masters	6 (33·3%)	
Years of Experience		
As a physiotherapist, mean (SD)	15·62 (7·38)	
In neurology/neurorehabilitation, mean (SD)	12·26 (7·65)	
Knowingly treating patients with FMD, mean (SD)	9·56 (7·01)	
Multidisciplinary support when treating people with FMD[a]	**Yes**	**No**
Psychiatry/Neuropsychiatry?	9 (52·9%)	8 (47·1%)
Neurology?	16 (94·1%)	1 (5·9%)
Physiotherapy peers/seniors?	14 (82·4%)	3 (17·6%)
Occupational Therapy?	9 (52·9%)	8 (47·1%)
Speech Therapy?	5 (29·4%)	12 (70·6%)
Social Work?	2 (11·8%)	15 (88·2%)
Specialist Nurses?	1 (5·9%)	16 (94·1%)
Have you completed additional Training?	**Yes**	**No**
In psychological interventions?	[b]3 (17·6%)	14 (82·4%)
Other training that helps you treat patients with FMD?	[c]6 (35·3%)	11 (64·7%)

[a]Missing data from one physiotherapist

[b]Additional Psychological training received by 3 physiotherapists' were

- 2-day CBT course
- 2-day motivational interviewing course
- Masters' in CBT and EMDR trained
- Postgraduate diploma in Health Behaviour Change and Motivational Interviewing

[c]Other Training courses that physiotherapists had completed that they felt helped with FMD

- 2-day FND Rehabilitation Course
- Chronic pain management training
- Masters' Module in Metal Health Skills,
- Bobath (Physiotherapy) training
- Functional Electrical Stimulation
- Advanced Communication Course
- Balance Rehabilitation
- Parkinson's Warrior (Exercise for Parkinson's disease)

15. Assessment of Specialist Physiotherapy Intervention Fidelity: Review of completed workbooks

We assessed copies of completed intervention workbooks as a measure of intervention fidelity. Each component of the intervention is represented in the workbook with space to answer questions and make notes. It is filled in during the treatment sessions by both the participant and physiotherapist. It therefore provides a record of the content of sessions. Written entries in the workbook sections was taken as evidence that the treatment component was addressed. The physiotherapists delivering the specialist physiotherapy intervention were required to take a copy of the completed workbook at the end of treatment, redact identifiable notes and send the copy to the central trial office.

125 completed workbook copies were received and assessed.

- 70% of all participants randomised to specialist physiotherapy (n=179)
- 83·9% of participants who completed at least 6 sessions (n=149)

Supplementary table 15.1 Evidence of use of the four main sections, N=125

	n
Treatment Planning	122 (97·6%)
Reflections	123 (98·4%)
Posture and movement	108 (86·4%)
Self-management	118 (94·4%)

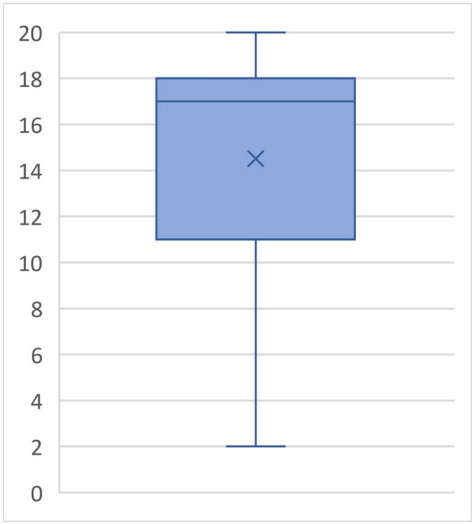
n=119 (95·2%) used at least 3 out of 4 sections
n=102 (81·6%) used all 4 sections

Completeness score

A completeness score was calculated for each workbook, based on the use of the 20 interactive pages in the workbook. The maximum score was 20. Not all pages are necessarily relevant to all participants, for example, pages relating to understanding and managing pain will not have been completed if the participant did not experience persistent pain. For the participant reflection pages (diary/reflection of sessions), completion of 3 or more reflections was considered evidence of use.

Supplementary table 15.2 Completeness score

	Completeness Score
Mean (SD)	14·5 (4·9)
Median (IQR)	17 (11 – 18)
Max	20
Min	2
Mode	19



16. Assessment of Specialist Physiotherapy Intervention Fidelity: Physiotherapist treatment checklist

The physiotherapists delivering the specialist physiotherapy completed a treatment checklist for each participant. See over the page for a copy of the log. As components of the intervention were completed, the physiotherapist noted which sessions addressed that component.

Excluding COIVD Group C (participants unable to receive timely treatment due to COVID-19 lockdown), n=152 participants were randomised to specialist physiotherapy

- n=140 (92·1%) started treatment and completed at least one session
- n=137 (90·1%) completed 6 sessions or more, the minimum number prespecified as a 'full dose'
- n=117 (77·0%) completed all 9 sessions, as described in the treatment protocol

Missed Sessions
Did the participant complete all planned sessions (data available from 132 participants)
Yes, n=116 (87·9%); No, n=16 (12·1%)

Supplementary table 16.1 Reasons for missing sessions

Reasons for missing sessions	Frequency
Fatigue, pain, and or headache	4
Not clinically needed	3
Participant requested to stop	2
No reason given	2
Family unwell	1
Unable to make session time	1
Anxiety	1
COVID-19 infection	1
Admin error	1

Supplementary table 16.2 Components of the intervention completed (n=133)
Note that not all treatment components are relevant to all participants.

	Number completing
Subjective History	133 (100%)
Physical Assessment	133 (100%)
Symptoms assessed	133 (100%)
Mobility observed	132 (99·2%)
Video of movement	131 (98·5%)
Goals	132 (99·2%)
Education	
Symptom model	132 (99·2%)
A leg to stand on	124 (93·2%)
Rationale for Physio4FMD	131 (98·5%)
Exploration of Movement	
Exacerbation & easing	130 (97·7%)
Activities and Postures	130 (97·7%)
Video analysed with participant	127 (95·5%)
Movement and Posture Retraining	
Habitual postures	125 (94·0%)
Sit to stand	120 (90·2%)

Gait	122 (91·7%)
Arms and hands	94 (70·7%)
On/off floor	65 (48·9%)
Stairs	68 (51·1%)
Treatment Adjuncts	
Mirror feedback	121 (91·0%)
Treadmill	75 (56·4%)
Electrical muscle stimulation	2 (1·5%)
Other	34 (25·6%)
Medication (education)	102 (76·7%)
Fatigue	
Education	122 (91·7%)
Management strategies	118 (88·7%)
Persistent Pain	
Education	98 (73·7%)
Management strategies	91 (68·4%)
Boom and Bust	
Education	122 (91·7%)
Management strategies	123 (92·5%)
Planning timetabling	112 (84·2%)
Memory and Concentration	101 (75·9%)
Bringing it Altogether	124 (93·2%)
Follow-up Planned	88 (66·2%)

Physio 4FMD Physiotherapy Treatment Checklist

Physiotherapist				**Site**				
Patient Initials				**No. of sessions completed**				
Date of first session				**Date of last session**				
Dominant Symptom (tick)	Weakness	Tremor	Gait	Jerks	Dystonia	Mixed	Fixed Dyst.	Other:

	SESSION NUMBERS WHEN ADDRESSED (or NA)
Initial Assessment: Subjective History	
▪ Following basic structure of initial assessment form	
Initial Assessment: Physical Examination	
▪ Symptoms assessed	
▪ Mobility observed	
▪ Video of movement	
Treatment Goals	
▪ Patient's priorities for treatment discussed	
Education	
▪ Diagnosis explained using symptom model	
▪ Discuss "A Leg to Stand On"	
▪ Discuss rationale for Physio4FMD	
Exploration of Movement	
▪ Exacerbating, easing and distractibility noted	
▪ Activities and postures assessed	
▪ Videos analysed and discussed with patient	
Movement and Posture Retraining	
▪ Habitual postures & sitting positions	
▪ Sit to stand to sit	
▪ Gait / walking	
▪ Arms and hands	
▪ Practice with/without walking aids	
▪ Getting on and off the floor	
▪ Stairs	
Treatment Adjuncts	
▪ Mirror	
▪ Treadmill	
▪ Electrical stimulation (FES/TENS)	
▪ Other (please state):	
Medication	
▪ Discussion with patient	
Fatigue	
▪ Education	
▪ Discussion of management strategies	
Persistent Pain	
▪ Education	
▪ Discussion of management strategies	
Boom & bust	
▪ Education	
▪ Discussion of management strategies	
▪ Activity planning & timetables	
Memory and Concentration	
▪ Education	
Bringing it all together – Winding up Treatment	
▪ Self-management plan completed	
Three month follow-up	
▪ Date planned	

Screenshot relevant pages of participant's workbook ☐

Did the patient complete all planned sessions? Yes No

If no, how many sessions were planned? _____ How were completed? _____

What was the reason for missed sessions? _____

Did the patient report any adverse effects from physiotherapy?

If yes, please describe below.

Please note that serious adverse events need to be reported via the SAE Reporting Form within 24 hours. See Investigator Pharmacovigilance SOP in your Investigator Site File for more information.

Describe Adverse Effect	Session Reported (1-9)	Has this been reported in the eCRF?

17. Treatment description: Participant reported description of treatment

Supplementary table 17.1 Data from telephone questionnaire (Groups A, B, and D)

	Treatment as usual	Specialist physiotherapy
How many sessions of physiotherapy did you receive?		
Number with available data	88 (83·0%)	128 (90·8%)
Mean (SD)	5·26 (7·49)	8·62 (2·40)
Median (IQR)	4 (2-7)	9 (8-9)
Approximately, how frequently did you attend physiotherapy? frequency (%)		
Number with available data	75 (70·7%)	123 (87·2%)
More than once a week	3 (4·0%)	112 (91·1%)
Weekly	16 (21·3%)	9 (7·3%)
Fortnightly	26 (34·7%)	2 (1·6%)
Monthly	22 (29·3%)	0 (0·0%)
Less than monthly	3 (4·0%)	0 (0·0%)
One session only	5 (6·7%)	0 (0·0%)
Please estimate the average length of sessions, frequency (%)		
Number with available data	73 (68·9%)	123 (87·2%)
20 mins or less	8 (10·9%)	0 (0·0%)
30 – 40 mins	30 (41·1%)	0 (0·0%)
45 – 60 mins	14 (19·2%)	4 (3·2%)
60 mins	18 (24·6%)	82 (66·7%)
75 mins or longer	3 (4·1%)	37 (30·1%)

Supplementary table 17.2 Treatment content, treatment as usual compared to specialist physiotherapy (Groups A, B, and D)

	Treatment as usual	Specialist physiotherapy
Did you receive printed material about FMD? Frequency (%)		
Number with available data	75 (70·7%)	121 (85·8%)
Yes	52/75 (69·3%)	120 (99·2%)
Was this a list of exercises only? "Yes"	37/49 (75·5%)	6/72 (8·3%)
Was this information about FMD?, "Yes"	13/46 (28·2%)	67/77 (87·0%)
Did the material ask questions about your symptoms?, "Yes"	12/53 (22·6%)	98/99 (99·0%)
Did you refer back to it after completing physiotherapy?, "Yes"	38/50 (76·0%)	103/116 (88·8%)
Did your physiotherapist spend time trying to help you understand your movement problem? Frequency (%)		
Number with available data	74 (69·8%)	122 (86·5%)
Yes	49 (66·2%)	121 (99·2%)
Did your physiotherapist talk about how focusing on movement can make movement worse? Frequency (%)		
Number with available data	74 (69·8%)	122 (86·5%)
Yes	75 (60·8%)	119 (97·5%)
Did you use any of the following exercise equipment in physiotherapy? Frequency (%)		
Number with available data	60 (56·7%)	121 (85·8%)
Weights	8 (13·3%)	6 (4·9%)
Elastic bands	14 (23·3%)	6 (4·9%)

Exercise bike	20 (33·3%)	3 (2·5%)
Treadmill	12 (20·0%)	67 (55·4%)
Gym/Swiss ball	18 (30·0%)	32 (26·4%)
Mirror	11 (18·3%)	97 (80·2%)
Electrical stimulation	2 (3·3%)	2 (1·6%)
Did your physiotherapist give you a walking aid? Frequency (%)		
Number with available data	75 (70·7%)	122 (86·5%)
Yes	15 (20·0%)	9 (7·4%)
If yes, did you have a walking aid already? "Yes"[a]	7/15 (46·7%)	6/9 (66·7%)
Did your physiotherapist give you an orthotic device or splint? Frequency (%)		
Number with available data	75 (70·7%)	122 (86·5%)
Yes	6 (8·0%)	2 (1·6%)
If yes, did you have a device already? "Yes", frequency[a]	3/6 (50·0%)	0/2 (0·0%)
At the time of your physiotherapy, were you experiencing regular pain? Frequency (%)		
Number with available data	74 (69·8%)	121 (85·6%)
Yes	62 (83·8%)	97 (80·2%)
If yes, did your physiotherapist try to help? "Yes"	30/62 (48·4%)	88/97 (90·7%)
At the time of your physiotherapy, were you experiencing regular fatigue? Frequency (%)		
Number with available data	75 (70·7%)	122 (86·5%)
Yes	68 (90·7%)	115 (94·3%)
If yes, did your physiotherapist try to help? "Yes"	40/68 (58·8%)	113/115 (98·3%)
At the time of your physiotherapy, did you take medication because of your movement problem (or symptoms related to FND)? Frequency (%)		
Number with available data	75 (70·7%)	122 (86·5%)
Yes	42 (56·0%)	69 (56·5%)
If yes, did your physiotherapist try to help? "Yes"	14/42 (33·3%)	58/69 (84·1%)
At the time of your physiotherapy, were you experiencing problems with memory and concentration? Frequency (%)		
Number with available data	75 (70·7%)	122 (86·5%)
Yes	53 (70·7%)	108 (88·5%)
If yes, did your physiotherapist try to help? "Yes"	21/53 (39·6%)	98/108 (90·7%)
With your physiotherapist's advice, did you make a plan to help you to continue to improve or stay improved? Frequency (%)		
Number with available data	73 (68·9%)	122 (86·5%)
Yes	48 (65·7%)	119 (97·5%)

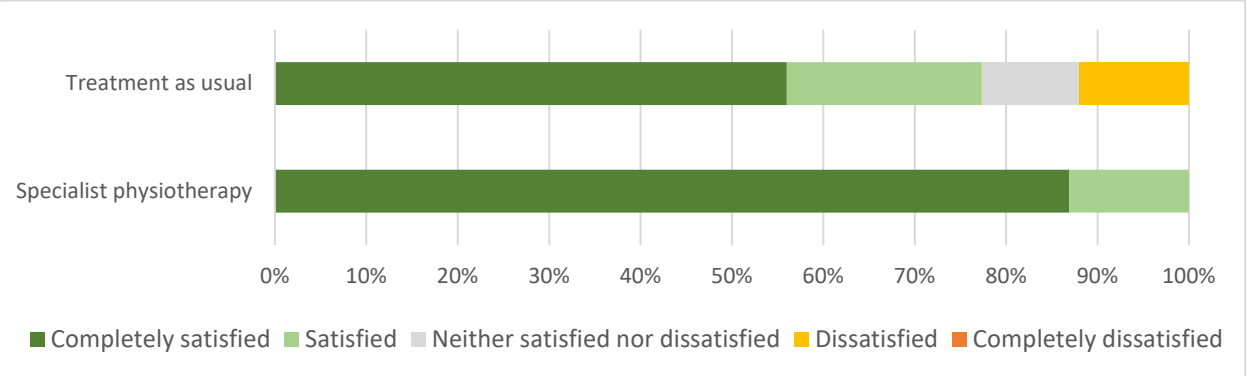
[a] for some of these cases the new device may have been a progression to a less supportive device, for example from a walking frame to a crutch

18. Satisfaction with Physiotherapy

Groups ABD

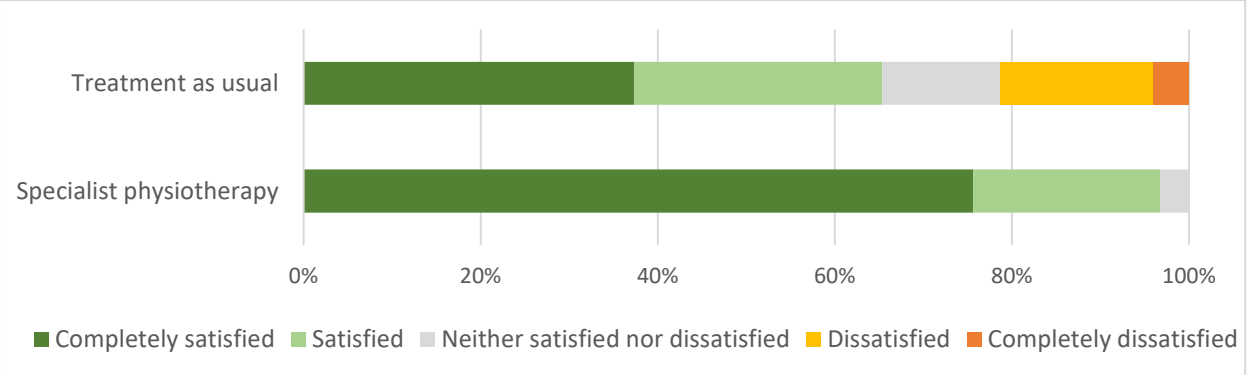
Supplementary table 18.1 How satisfied were you with the **person** who gave you physiotherapy?

	Specialist physiotherapy		Treatment as usual	
Participants with available data	122	86·5%	75	70·8%
Completely satisfied	106	86·9%	42	56·0%
Satisfied	16	13·1%	16	21·3%
Neither satisfied nor dissatisfied	0	0·0%	8	10·7%
Dissatisfied	0	0·0%	9	12·0%
Completely dissatisfied	0	0·0%	0	0·0%



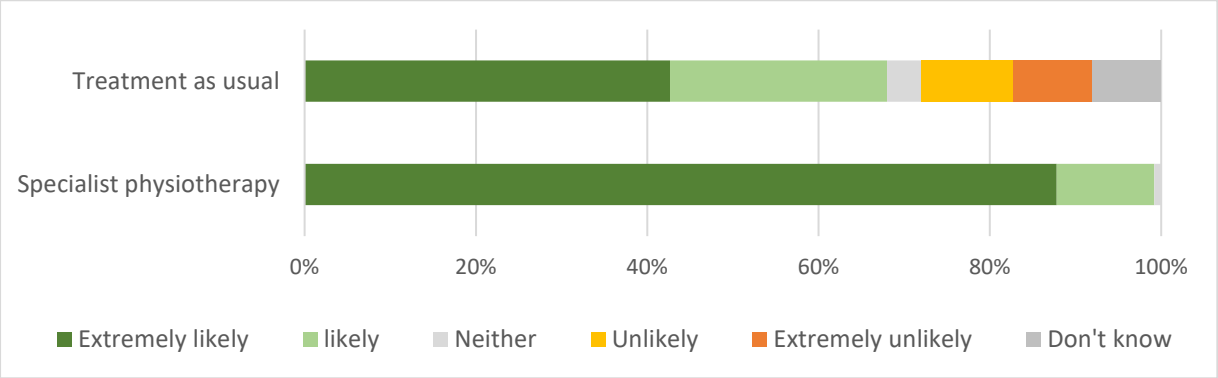
Supplementary table 18.2 Overall, how satisfied were you with the **physiotherapy** you received?

	Specialist physiotherapy		Treatment as usual	
Participants with available data	123	87·2%	75	70·8%
Completely satisfied	93	75·6%	28	37·3%
Satisfied	26	21·1%	21	28·0%
Neither satisfied nor dissatisfied	4	3·3%	10	13·3%
Dissatisfied	0	0·0%	13	17·3%
Completely dissatisfied	0	0··0%	3	4·0%



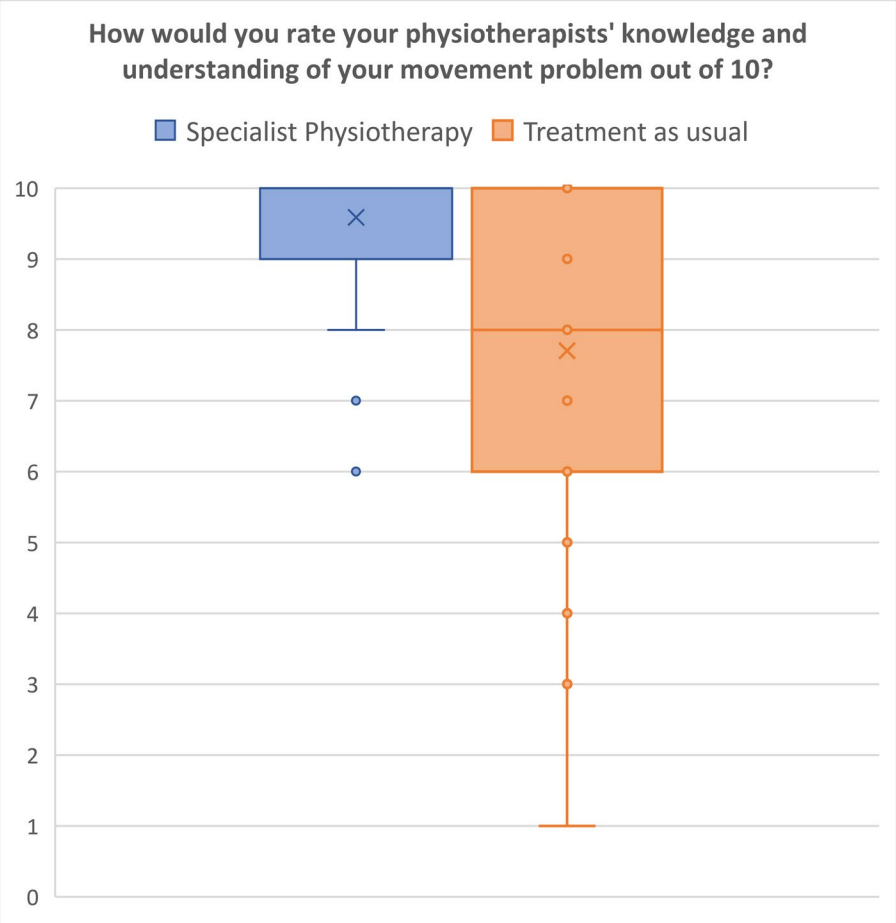
Supplementary table 18.3 How likely are you to **recommend** the treatment you received to family and friends if they need similar treatment?

	Specialist physiotherapy		Treatment as usual	
Participants with available data	123	87·2%	69	70·8%
Extremely likely	108	87·8%	32	42·7%
likely	14	11·4%	19	25·3%
Neither	1	0·8%	3	4·0%
Unlikely	0	0·0%	8	10·7%
Extremely unlikely	0	0·0%	7	9·3%
Don’t know	0	0·0%	6	8·0%



Supplementary table 18.4 How would you rate your physiotherapists' **knowledge and understanding** of your movement problem out of 10?

	Specialist physiotherapy	Treatment as usual
Participants with available data	123 (87·2%)	75 (70·8%)
Mean (SD)	9·6 (0·81)	7·7 (2·29)
Median (IQR)	10 (9 – 10)	8 (6 – 10)
Mode	10	10
Min	6	1
Max	10	10

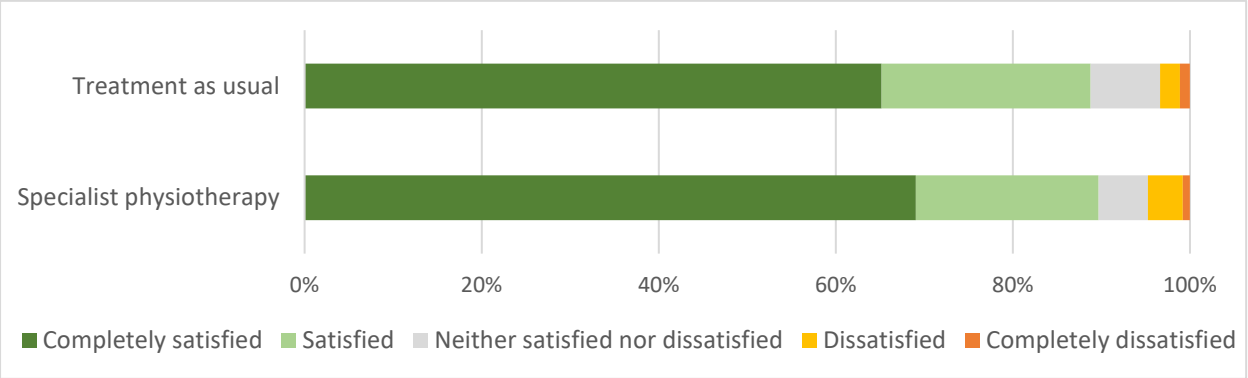


19. Satisfaction with Neurology Input

Groups ABD

Supplementary table 19.1 How satisfied were you with the **neurologist** who referred you into the study?

	Specialist physiotherapy		Treatment as usual		Combined groups	
Participants with available data	126	89·4%	89	84·0%	215	87·0%
Completely satisfied	87	69·0%	58	65·2%	145	67·4%
Satisfied	26	20·6%	21	23·6%	47	21·9%
Neither satisfied nor dissatisfied	7	5·6%	7	7·9%	14	6·5%
Dissatisfied	5	4·0%	2	2·2%	7	3·3%
Completely dissatisfied	1	0·8%	1	1·1%	2	0·9%



Group C (Did not receive their physiotherapy treatment due to the impact of COVID-19 lockdown)

Supplementary table 19.2 How satisfied were you with the **neurologist** who referred you into the study?

	Specialist physiotherapy		Treatment as usual		Combined groups	
Participants with available data	24	88·9%	58	93·5%	82	92·1%
Completely satisfied	18	75·0%	35	60·3%	53	64·6%
Satisfied	2	8·3%	14	24·1%	16	19·5%
Neither satisfied nor dissatisfied	2	8·3%	3	5·2%	5	6·1%
Dissatisfied	2	8·3%	5	8·6%	7	8·5%
Completely dissatisfied	0	0·0%	1	1·7%	1	1·2%

20. Primary outcome completion method

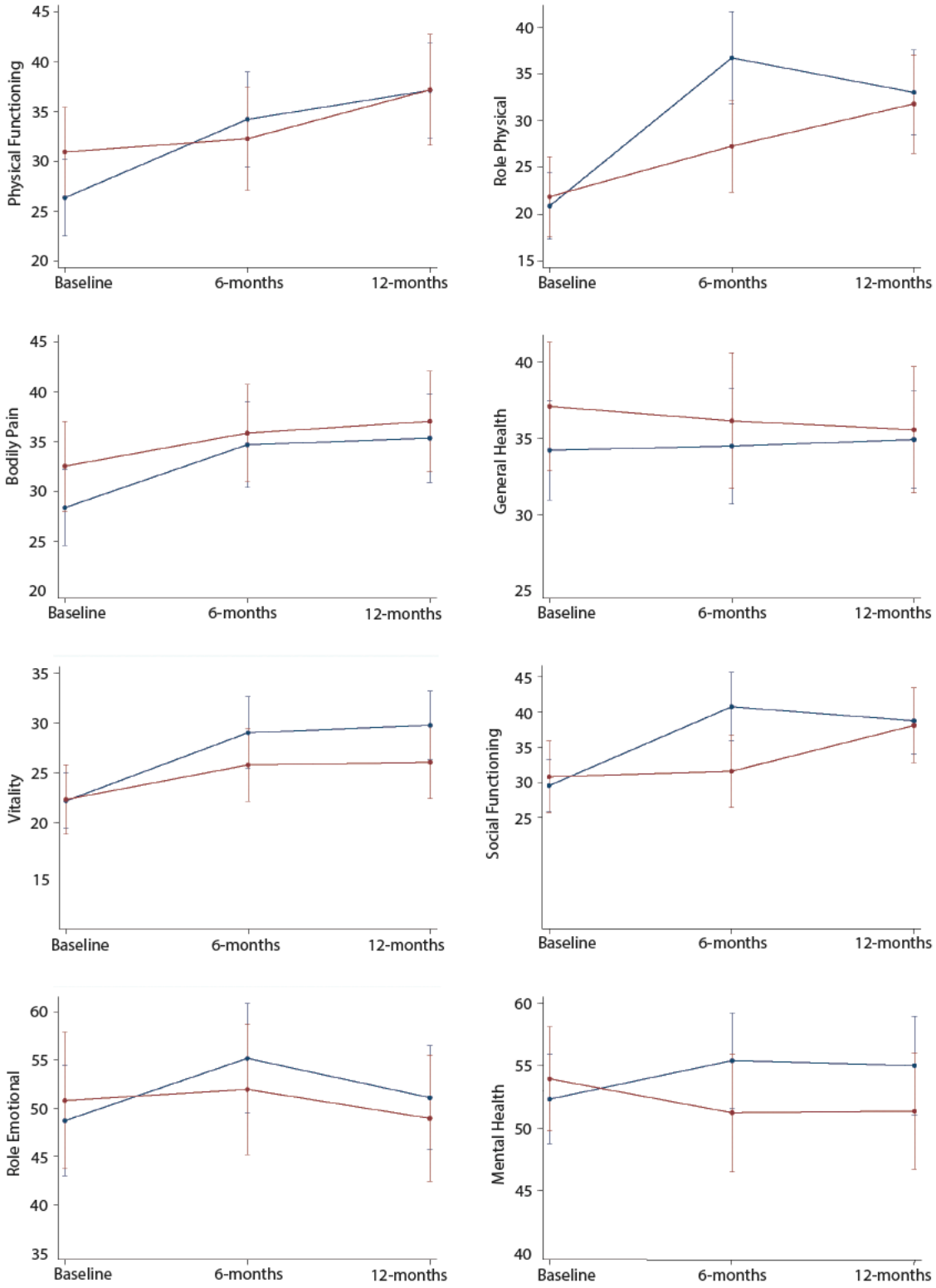
The trial participants chose their preferred method of completing the primary outcome out of online form, paper and pen by return post, or over the telephone with a blinded research assistant. The method of completion by randomised group is presented below.

Supplementary table 20.1 Primary outcome completion method

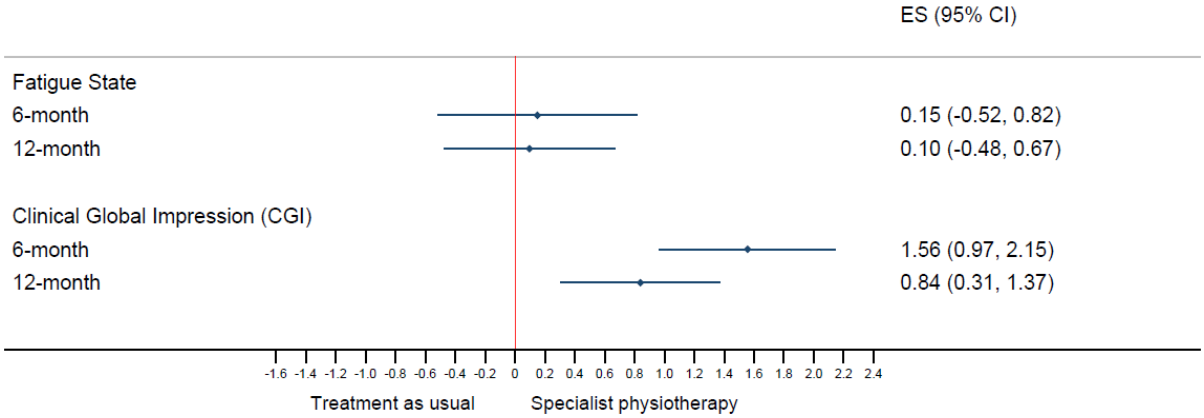
	Specialist physiotherapy	**Treatment as usual**
Online	102 (57·0%)	100 (56·8%)
Return post	28 (15·6%)	26 (14·8%)
Telephone	29 (16·3%)	32 (18·2%)
Missing	20 (11·2%)	18 (10·2%)
TOTAL	179 (100%)	176 (100%)

21. Primary and secondary outcome figures

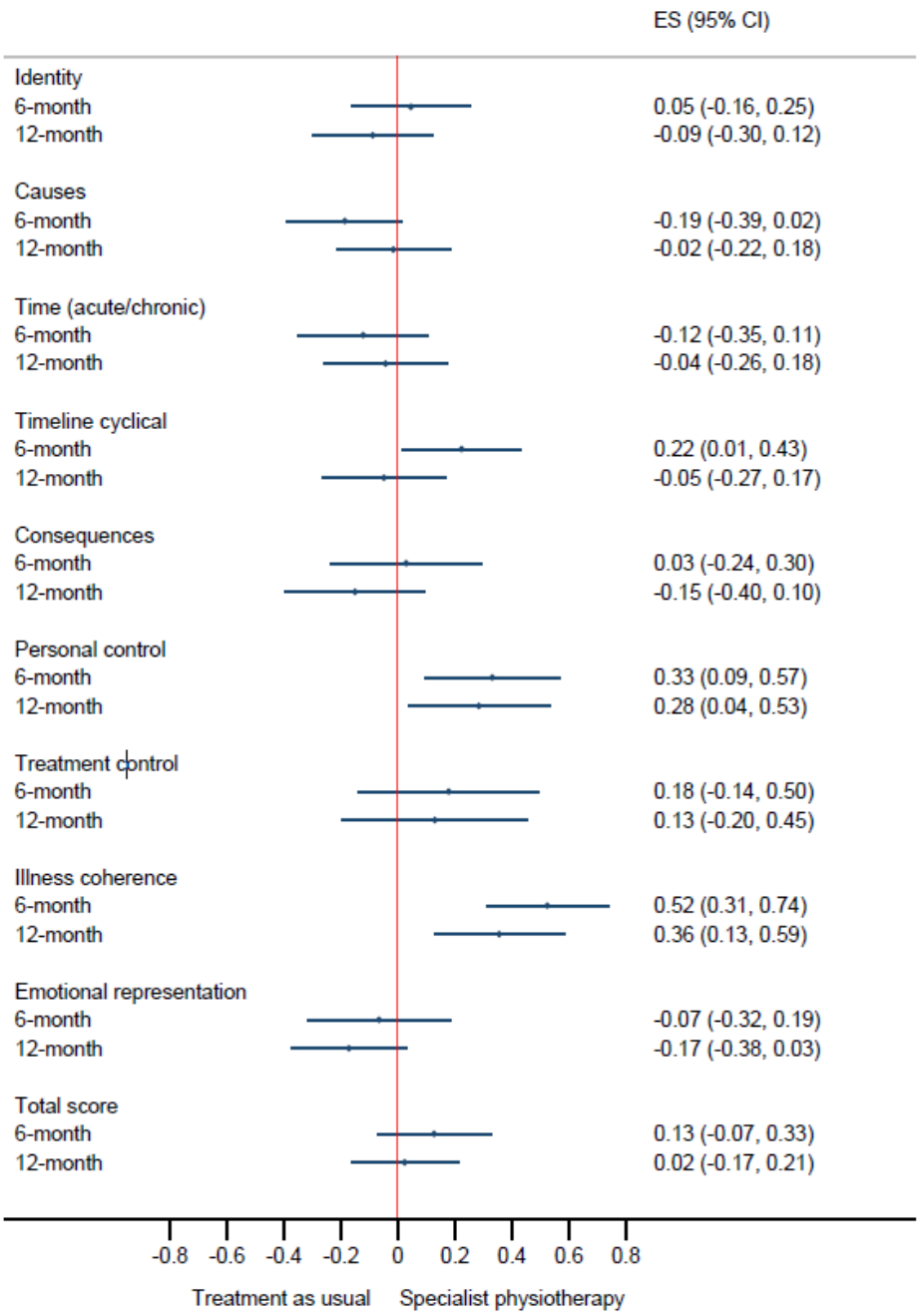
Supplementary figure 21.1 Short Form 36 Plots
Blue line: specialist physiotherapy, red line: treatment as usual



Supplementary figure 21.2 Categorical outcome measures, effect size (ES) and 95% confidence interval (CI) at six and 12-months.



Supplementary figure 21.3 Revised Illness Perception Questionnaire (R-IPQ), effect size (ES) and 95% confidence interval (CI) at six and 12-months.



Legend:
Identify: Perception that symptoms are associated with a specific label.
Causes: Ideas about likely causes.
Timeline (acute/chronic): Beliefs about duration of illness.
Timeline cyclical: Beliefs about the cyclical or recurrent nature of illness.
Consequences: Beliefs about the impact of illness on quality of life.
Personal control: Beliefs about confidence in ability to control symptoms.
Treatment control: Beliefs about effectiveness of treatment in improving symptoms.
Illness coherence: Belief about holding a logical understanding of the illness/symptoms.
Emotional representation: Emotional distress related to illness/symptoms.

22. Secondary outcome: NHS Digital Data

Hospital Episode Statistics (from NHS England) and Information Services Division data (from NHS Scotland).

Digital data held by NHS England and NHS Scotland on the number of hospital admissions, days admitted, accident and emergency (A&E) attendances, and hospital outpatient appointments was collected for all participants for the 12-months before recruitment and 12-months post recruitment/randomisation.

The data was analysed using mixed effects negative binomial regression with a random effect for physiotherapist and clusters of 1 in the treatment as usual group (same as for main analysis). The models controlled for baseline count of the outcome. Incident rate ratios (IRR) are reported (which are interpreted in a similar way to odds ratio). The null is 1, below 1, less likely to occur, above 1 more likely to occur.

Supplementary table 22.1 Health service use descriptive analysis (COVID groups ABD)

Health service use		Specialist physiotherapy (n=141)	Treatment as usual (n=106)
Inpatient days			
12 months to baseline	Median (IQR)	1 (0, 3)	1 (0, 4)
	Mean (SD)	4·41 (9·97)	3·87 (7·50)
12 months post randomisation	Median (IQR)	0 (0, 2)	0 (0, 1)
	Mean (SD)	3·03 (7·98)	3·80 (15·30)
Inpatient admissions			
12 months to baseline	Median (IQR)	1 (0, 2)	1 (0, 2)
	Mean (SD)	1·45 (2·72)	1·32 (3·29)
12 months post randomisation	Median (IQR)	0 (0, 1)	0 (0, 1)
	Mean (SD)	1·28 (2·34)	0·64 (1·35)
A&E attendance			
12 months to baseline	Median (IQR)	1 (0, 2)	1 (0, 2)
	Mean (SD)	1·76 (3·12)	1·28 (1·62)
12 months post randomisation	Median (IQR)	0 (0, 1)	0 (0, 1)
	Mean (SD)	1·27 (3·78)	0·83 (1·13)
Outpatient attendance			
12 months to baseline	Median (IQR)	5 (2, 8)	6 (3, 10)
	Mean (SD)	7·38 (9·94)	7·70 (7·39)
12 months post randomisation	Median (IQR)	5 (2, 9)	5 (2, 9)
	Mean (SD)	6·82 (7·02)	7·30 (8·56)

Supplementary table 22.2 Modelling health service use

Health Service Use	IRR	95% CI
Inpatient days 12 months post randomisation	1·67	(0·62, 4·49)
Inpatient admissions 12 months post randomisation	1·72	(0·95, 3·10)
A&E attendance 12 months post randomisation	0·99	(0·70, 1·41)
Outpatient attendance 12 months post randomisation	0·93	(0·67, 1·29)

23. Six- and 12-Month Assessment Outcomes, groups A, B and D

	Specialist physiotherapy n=152 maximum	Treatment as usual n=114 maximum	Difference adjusting for baseline (95% CI)
SF36 Physical Functioning, mean (SD) Scale range 0-100			
Baseline	26·3 (23·1)	30·9 (23·2)	
Participants with available data	141 (93%)	106 (93%)	
6-months	34·2 (27·9)	32·3 (25·6)	4·568 (-0·878, 10·013)
Participants with available data	134 (88%)	97 (85%)	
12-months	37·1 (28·4)	37·2 (28·5)	3·534 (-2·258, 9·325)[a]
Participants with available data	138 (91%)	103 (90%)	
SF36 Physical Role Limitations, mean (SD) Scale range 0-100			
Baseline	20·9 (21·3)	21·9 (22·2)	
Participants with available data	141 (93%)	106 (93%)	
6-months	36·7 (28·8)	27·3 (24·6)	**10·109 (3·716, 16·503)***
Participants with available data	134 (88%)	99 (87%)	
12-months	33·0 (26·9)	31·8 (27·0)	2·267 (-3·687, 8·221)
Participants with available data	138 (91%)	103 (90%)	
SF36 Bodily Pain, mean (SD) Scale range 0-100			
Baseline	28·4 (22·7)	32·6 (23·3)	
Participants with available data	141 (93%)	106 (93%)	
6-months	34·7 (25·3)	35·9 (24·5)	1·502 (-3·504, 6·509)
Participants with available data	134 (88%)	99 (87%)	
12-months	35·4 (26·4)	37·1 (25·6)	1·144 (-4·615, 6·902)
Participants with available data	138 (91%)	103 (90%)	
SF36 General Health Perceptions, mean (SD) Scale range 0-100			
Baseline	34·2 (19·4)	37·1 (21·7)	
Participants with available data	141 (93%)	106 (93%)	
6-months	34·5 (22·2)	36·1 (22·2)	0·058 (-4·017, 4·132)
Participants with available data	134 (95%)	99 (87%)	
12-months	34·9 (18·9)	35·5 (20·9)	1·796 (-1·977, 5·570)
Participants with available data	136 (89%)	103 (90%)	
SF36 Energy/Vitality, mean (SD) Scale range 0-100			
Baseline	22·2 (16·7)	22·3 (18·0)	
Participants with available data	141 (93%)	106 (93%)	
6-months	29·1 (21·2)	25·8 (18·2)	3·217 (-1·264, 7·699)
Participants with available data	134 (88%)	99 (87%)	
12-months	29·8 (20·3)	26·1 (18·7)	3·752 (-0·874, 8·377)
Participants with available data	137 (90%)	103 (90%)	
SF36 Social Functioning, mean (SD) Scale range 0-100			
Baseline	29·5 (22·6)	30·8 (26·5)	
Participants with available data	141 (93%)	106 (93%)	
6-months	40·8 (28·6)	31·6 (25·8)	**8·889 (2·560, 15·218)***
Participants with available data	134 (88%)	99 (87%)	
12-months	38·8 (27·7)	38·1 (27·5)	1·068 (-5·356, 7·492)
Participants with available data	137 (90%)	103 (90%)	

SF36 Emotional Role Limitations, mean (SD) Scale range 0-100			
Baseline	48·7 (34·3)	50·8 (36·8)	
Participants with available data	141 (93%)	106 (93%)	
6-months	55·2 (33·3)	51·9 (33·9)	3·459 (-2·991, 9·910)
Participants with available data	134 (88%)	99 (87%)	
12-months	51·1 (32·0)	48·9 (33·5)	3·638 (-2·850, 10·126)
Participants with available data	138 (91%)	103 (90%)	
SF36 Mental Health, mean (SD) Scale range 0-100			
Baseline	52·3 (21·5)	54·0 (21·7)	
Participants with available data	141 (93%)	106 (93%)	
6-months	55·4 (22·6)	51·3 (23·7)	**5·046 (0·482, 9·611)***
Participants with available data	134 (88%)	99 (87%)	
12-months	55·1 (23·3)	51·4 (23·9)	**5·360 (0·940, 9·779)***
Participants with available data	137 (90%)	103 (90%)	
Participant rated Clinical Global Impression Scale of Improvement (frequency)			
6-month			
Participants with available data	134 (88%)	96 (84%)	
Much Improved	29 (21·6%)	5 (5·2%)	
Improved	55 (41·0%)	22 (22·9%)	
No Change	40 (29·9)	59 (61·5%)	
Worse	7 (5·2%)	8 (8·3%)	
Much Worse	3 (2·2%)	2 (2·1%)	
Odds ratio of improving (95% CI)[b]			**4·745 (2·630, 8·564)***
12-month			
Participants with available data	138 (91%)	102 (89%)	
Much Improved	36 (26·1%)	14 (13·7%)	
Improved	45 (32·6%)	25 (24·5%)	
No Change	41 (29·7%)	47 (46·1%)	
Worse	12 (8·7%)	10 (9·8%)	
Much Worse	4 (2·9%)	6 (5·9%)	
Odds ratio of improving (95% CI)[b]			**2·315 (1·361, 3·938)***
Functional Mobility Scale, mean (SD) [c] Scale range 3-18			
Baseline	11·4 (4·5)	11·5 (4·4)	
Participants with available data	140 (92%)	104 (91%)	
6-months	12·0 (4·6)	11·5 (4.4)	0·540 (-0·199, 1·279)
Participants with available data	134 (88%)	97 (85%)	
12-months	12·2 (4·5)	11·9 (4·6)	0·598 (-0·198, 1·395)
Participants with available data	136 (89%)	97 (85%)	
Hospital Anxiety and Depression Scale: Anxiety, mean (SD) [d] Scale Range 0-21			
Baseline	10·3 (5·0)	9·5 (5·2)	
Participants with available data	140 (92%)	105 (92%)	
6-months	9·9 (5·2)	10·2 (5·3)	-1·053 (-1·971, -0·135)
Participants with available data	134 (88%)	97 (85%)	
12-months	10·0 (5·2)	9·4 (4·9)	-0·531 (-1·412, 0·350)
Participants with available data	135 (89%)	97 (85%)	
Hospital Anxiety and Depression Scale: Depression, mean (SD) [d] Scale Range 0-21			

Baseline	8·8 (4·1)	8·3 (4·4)	
Participants with available data	140 (92%)	105 (92%)	
6-months	8·0 (4·7)	8·5 (4·7)	-0·561 (-1·578, 0·456)
Participants with available data	134 (88%)	97 (85%)	
12-months	8·5 (4·7)	8·2 (4·8)	-0·203 (-1·200, 0·795)
Participants with available data	135 (89%)	97 (85%)	
Fatigue 5-point scale (frequency)			
Baseline			
Participants with available data	141 (93%)	106 (93%)	
No tiredness/fatigue	3 (2·1%)	2 (1·9%)	
Slight	12 (8·5%)	16 (15·1%)	
Moderate	68 (48·2%)	35 (33·0%)	
Severe	42 (29·8%)	38 (35·9%)	
Extreme	16 (11·4%)	15 (14·2%)	
6-month			
Participants with available data	134 (88%)	97 (85%)	
No tiredness/fatigue	5 (3·7%)	1 (1·0%)	
Slight	13 (9·7%)	10 (10·3%)	
Moderate	42 (31·3%)	30 (30·9%)	
Severe	42 (31·3%)	37 (39·1%)	
Extreme	32 (23·9%)	19 (19·6%)	
Odds ratio of milder fatigue (95%CI)[c]			1·163 (0·596, 2·269)
12-month			
Participants with available data	136 (89%)	97 (85%)	
No tiredness/fatigue	5 (3·7%)	14 (14·4%)	
Slight	18 (13·2%)	32 (33·0%)	
Moderate	44 (32·4%)	36 (37·1%)	
Severe	36 (26·5%)	13 (13·4%)	
Extreme	33 (24·3%)	14 (14·4%)	
Odds ratio of milder fatigue (95% CI)[e]			1·102 (0·621, 1·955)
Confidence in the diagnosis, mean (SD) Scale range 0-10			
Baseline	8·1 (2·0)	8·0 (2·2)	
Participants with available data	141 (93%)	106 (93%)	
6-months	8·1 (2·3)	7·0 (2·8)	**1·086 (0·541, 1·631)***
Participants with available data	132 (87%)	97 (85%)	
12-months	8·1 (2·3)	7·4 (2·8)	**0·781 (0·193, 1·369)***
Participants with available data	134 (88%)	94 (82%)	
Revised Illness Perception Questionnaire, mean (SD)			
Scale range 0-14			
Identity Baseline	9·0 (2·7)	8·6 (2·9)	
Participants with available data	139 (91%)	105 (92%)	
Identity 6-months	9·3 (2·8)	9·0 (3·0)	0·126 (-0·459, 0·710)
Participants with available data	133 (87%)	96 (84%)	
Identity 12-months	9·3 (2·7)	9·1 (3·0)	-0·247 (-0·839, 0·345)
Participants with available data	132 (87%)	94 (82%)	
Scale range 18-90			
Causes Baseline	40·8 (10·4)	40·9 (12·0)	
Participants with available data	139 (91%)	105 (92%)	
Causes 6-months	40·6 (8·8)	43·0 (12·0)	-2·069 (-4·325, 0·187)
Participants with available data	133 (87%)	96 (84%)	
Causes 12-months	42·0 (10·2)	41·7 (10·6)	-0·183 (-2·404, 2·038)
Participants with available data	132 (87%)	94 (82%)	

Scale range 6-30			
Timeline Baseline	20·6 (4·4)	20·3 (4·5)	
Participants with available data	140 (92%)	106 (93%)	
Timeline 6-months	22·2 (5·1)	21·8 (4·3)	-0·547 (-1·570, 0·476)
Participants with available data	133 (87%)	95 (83%)	
Timeline 12-months	22·8 (4·5)	22·2 (4·0)	-0·194 (-1·175, 0·787)
Participants with available data	132 (87%)	94 (82%)	
Scale range 4-20			
Timeline cyclical Baseline	14·2 (3·7)	14·0 (3·95)	
Participants with available data	141 (93%)	106 (93%)	
Timeline cyclical 6-months	14·3 (3·3)	13·4 (3·8)	**0·852 (0·054, 1·651)***
Participants with available data	133 (87%)	96 (84%)	
Timeline cyclical 12-months	13·7 (3·7)	13·7 (3·7)	-0·188 (-1·021, 0·644)
Participants with available data	133 (87%)	94 (82%)	
Scale range 6-30			
Consequences Baseline	24·0 (4·0)	23·9 (3·6)	
Participants with available data	140 (92%)	105 (92%)	
Consequences 6-months	23·3 (4·1)	23·3 (3·6)	0·109 (-0·906, 1·124)
Participants with available data	133 (87%)	96 (84%)	
Consequences 12-months	22·6 (4·5)	22·8 (4·0)	-0·573 (-1·508, 0·362)
Participants with available data	132 (87%)	94 (82%)	
Scale range 6-30			
Personal control Baseline	18·6 (4·0)	19·7 (3·8)	
Participants with available data	140 (92%)	105 (92%)	
Personal control 6-months	19·4 (4·5)	18·8 (4·1)	**1·294 (0·367, 2·220)***
Participants with available data	132 (87%)	96 (84%)	
Personal control 12-months	19·4 (4·4)	19·0 (4·2)	**1·108 (0·138, 2·079)**
Participants with available data	133 (87%)	94 (82%)	
Scale range 5-25			
Treatment control Baseline	16·3 (2·6)	16·9 (2·6)	
Participants with available data	140 (92%)	105 (92%)	
Treatment control 6-months	15·9 (3·6)	15·8 (3·4)	0·466 (-0·367, 1·299)
Participants with available data	133 (87%)	96 (84%)	
Treatment control 12-months	15·7 (3·7)	15·9 (3·5)	0·339 (-0·512, 1·190)
Participants with available data	133 (87%)	94 (82%)	
Scale range 5-25			
Illness coherence Baseline	13·3 (4·7)	13·7 (4·7)	
Participants with available data	141 (93%)	106 (93%)	
Illness coherence 6-months	17·0 (4·5)	14·7 (4·7)	**2·460 (1·456, 3·464)***
Participants with available data	133 (87%)	96 (84%)	
Illness coherence 12-months	17·2 (4·9)	15·6 (5·0)	**1·669 (0·592, 2·745)***
Participants with available data	133 (87%)	94 (82%)	
Scale range 6-30			
Emotional representation Baseline	21·4 (5·3)	20·4 (5·3)	
Participants with available data	141 (93%)	106 (93%)	
Emotional representation 6-months	19·8 (5·7)	19·6 (5·2)	-0·355 (-1·692, 0·982)
Participants with available data	133 (87%)	96 (84%)	
Emotional representation 12-months	19·5 (5·5)	19·6 (4·7)	-0·911 (-1·999, 0·176)
Participants with available data	133 (87%)	94 (82%)	

Scale range 56-294			
TOTAL Baseline	176·0 (16·8)	175·5 (21·6)	
Participants with available data	133 (87%)	102 (89%)	
TOTAL 6-months	178·2(17·2)	175·6 (18·7)	1·927 (-1·892, 5·745)
Participants with available data	132 (87%)	95 (83%)	
TOTAL 12-months	178·0 (17·9)	176·2 (19·5)	0·171 (-3·422, 3·764)
Participants with available data	129 (85%)	94 (82%)	
Extended Patient Health Questionnaire, mean (SD) Scale range 0-31			
Assessed at baseline only	16·9 (5·7)	15·7 (5·7)	
Participants with available data	135 (89%)	105 (92%)	
EQ-5D-5L – Value set for England, mean (SD) Scale range 0-1			
Baseline	0·424 (0·290)	0·462 (0·264)	
Participants with available data	141 (93%)	106 (93%)	
6-months	0·492 (0·291)	0·452 (0·294)	**0·059 (0·002, 0·116)***
Participants with available data	134 (88%)	97 (85%)	
12-months	0·483 (0·324)	0·480 (0·270)	0·043 (-0·021, 0·106)
Participants with available data	137 (91%)	97 (85%)	
QALYs	0·475 (0·264)	0·476 (0·234))	0·035 (-0·007, 0·076)
Participants with available data	133 (88%)	93 (82%)	
EQ-5D-5L – 5L to 3L mapping, mean (SD) Scale range 0-1			
Baseline	0·310 (0·296)	0·354 (0·286)	
Participants with available data	141 (93%)	106 (93%)	
6-months	0·383 (0·311)	0·341 (0·310)	0·069 (-0·0004, 0·139)
Participants with available data	134 (88%)	97 (85%)	
12-months	0·370 (0·342)	0·368 (0·298)	0·049 (-0·020, 0·117)
Participants with available data	137 (91%)	97 (85%)	
QALYs	0·366 (0·281)	0·365 (0·254)	0·042 (-0·004, 0·073)
Participants with available data	133 (88%)	93 (82%)	

*Denotes a statistically significant difference.

[a] Intraclass correlation coefficient (ICC) = 0.017.

[b] Odds ratio of improving if assigned to specialist physiotherapy (much improved or improved vs no change, worse, or much worse).

[c] Functional Mobility Scale rates the assistance needed over three distances: 5 metres, 50 metres, 500 metres. Each distance is rated from 1-6: 1=uses wheelchair; 2=uses walker/frame; 3=uses crutches; 4=uses walking stick(s); 5=independent but needs to hold rail on stairs; 6=independent on all surfaces.

[d] HADS Anxiety and Depression cut-off score of 8+ has been found to have acceptable sensitivity and specificity for cases of anxiety and depression (Bjelland et al 2002)

[e] Odds ratio of milder fatigue if assigned to specialist physiotherapy (no or slight fatigue vs moderate, severe, or extreme).

Reference:

Bjelland, I., Dahl, A. A., Haug, T., & Neckelmann, D. (2002). The validity of the Hospital Anxiety and Depression Scale An updated literature review. *Journal of Psychosomatic Research*, *52*, 69–77.

24. Results table: Primary and secondary outcomes for group C

Supplementary table 24.1
(Includes those unassigned a COVID group due to withdrawal or loss to follow-up)

	Specialist physiotherapy n=38	Treatment as usual n=70
SF36 Physical Functioning, mean (SD)		
Baseline	27·4 (23·1)	25·5 (24·0)
Participants with available data	37 (97·4%)	70 (100%)
6-months	35·2 (23·6)	30·0 (27·9)
Participants with available data	29 (76·3%)	55 (78·6%)
12-months	32·1 (28·8)	28·9 (26·9)
Participants with available data	21 (55·3%)	54 (77·1%)
SF36 Physical Role Limitations, mean (SD)		
Baseline	22·7 (26·5)	22·1 (22·4)
Participants with available data	37 (97·4%)	70 (100%)
6-months	29·5 (27·3)	25·7 (24·6)
Participants with available data	29 (76·3%)	55 (78·6%)
12-months	29·5 (29·3)	29·7 (27·7)
Participants with available data	21 (55·3%)	54 (77·1%)
SF36 Bodily Pain, mean (SD)		
Baseline	28·7 (22·2)	30·5 (25·4)
Participants with available data	37 (97·4%)	70 (100%)
6-months	35·3 (24·9)	30·7 (19·1)
Participants with available data	29 (76·3%)	55 (78·6%)
12-months	38·2 (29·1)	33·8 (24·6)
Participants with available data	21 (55·3%)	54 (77·1%)
SF36 General Health Perceptions, mean (SD)		
Baseline	35·8 (21·8)	32·3 (20·1)
Participants with available data	37 (97·4%)	70 (100%)
6-months	32·3 (18·8)	32·5 (19·2)
Participants with available data	29 (76·3%)	54 (77·1%)
12-months	36·3 (22·3)	33·0 (19·6)
Participants with available data	21 (55·3%)	54 (77·1%)
SF36 Energy/Vitality, mean (SD)		
Baseline	22·4 (18·5)	18·9 (16·9)
Participants with available data	37 (97·4%)	70 (100%)
6-months	24·8 (17·5)	22·3 (17·3)
Participants with available data	29 (76·3%)	55 (78·6%)
12-months	22·3 (20·4)	19·0 (16·3)
Participants with available data	21 (55·3%)	54 (77·1%)
SF36 Social Functioning, mean (SD)		
Baseline	23·3 (23·0)	32·7 (28·5)
Participants with available data	37 (97·4%)	70 (100%)
6-months	30·6 (28·3)	36·8 (32·4)
Participants with available data	29 (76·3%)	55 (78·6%)
12-months	38·1 (35·9)	38·2 (32·4)
Participants with available data	21 (55·3%)	54 (77·1%)
SF36 Emotional Role Limitations, mean (SD)		
Baseline	41·0 (35·3)	46·3 (36·4)
Participants with available data	37 (97·4%)	70 (100%)
6-months	41·1 (29·3)	45·3 (34·7)
Participants with available data	29 (76·3%)	55 (78·6%)
12-months	45·6 (35·7)	45·5 (34·1)
Participants with available data	21 (55·3%)	54 (77·1%)
SF36 Mental Health, mean (SD)		

Baseline	44·2 (23·9)	49·6 (23·9)
Participants with available data	37 (97·4%)	70 (100%)
6-months	44·1 (23·1)	49·9 (23·2)
Participants with available data	29 (76·3%)	55 (78·6%)
12-months	46·4 (26·3)	51·0 (24·1)
Participants with available data	21 (55·3%)	54 (77·1%)
Participant rated Clinical Global Impression Scale of Improvement, frequency (%)		
6-month		
Participants with available data	27 (71·0%)	54 (77·1%)
Much Improved	0 (0·0%)	0 (0·0%)
Improved	1 (3·7%)	4 (7·4%)
No Change	20 (74·1%)	39 (72·2%)
Worse	5 (18·5%)	8 (14·8%)
Much Worse	1 (3·7%)	3 (5·6%)
Good outcome (Much Improved, or Improved)	1 (3·7%)	4 (7·4%)
Poor outcome (No Change, Worse, or Much Worse)	26 (96·3%)	50 (92·6%)
12-month		
Participants with available data	21 (55·3%)	50 (71·4%)
Much Improved	2 (9·5%)	2 (4·0%)
Improved	5 (23·8%)	6 (12·0%)
No Change	9 (42·9%)	32 (64·0%)
Worse	5 (23·8%)	7 (14·0%)
Much Worse	0 (0·0%)	3 (6·0%)
Good outcome (Much Improved, or Improved)	7 (33·3%)	8 (16·0%)
Poor outcome (No Change, Worse, or Much Worse)	14 (66·7%)	42 (84·0%)
Functional Mobility Scale, mean (SD)		
Baseline	11·2 (4·5)	11·6 (4·3)
Participants with available data	37 (97·4%)	70 (100%)
6-months	12·3 (4·8)	11·2 (4·5)
Participants with available data	28 (73·7%)	55 (78·6%)
12-months	12·1 (4·8)	10·8 (4·6)
Participants with available data	21 (55·3%)	52 (74·3%)
Hospital Anxiety and Depression Scale: Anxiety, mean (SD)		
Baseline	10·8 (5·7)	10·2 (5·3)
Participants with available data	38 (100%)	70 (100%)
6-months	10·5 (4·9)	10·8 (5·3)
Participants with available data	28 (73·7%)	54 (77·1%)
12-months	10·0 (5·6)	10·5 (4·9)
Participants with available data	21 (55·3%)	52 (74·3%)
Hospital Anxiety and Depression Scale: Depression, mean (SD)		
Baseline	9·4 (4·8)	8·8 (4·7)
Participants with available data	38 (100%)	70 (100%)
6-months	8·6 (5·1)	9·0 (4·7)
Participants with available data	28 (73·7%)	54 (77·1%)
12-months	9·7 (5·7)	9·5 (4·5)
Participants with available data	21 (55·3%)	52 (74·3%)
Fatigue (5-point scale), frequency (%)		
Baseline		

Participants with available data	38 (100%)	70 (100%)
No tiredness/fatigue	2 (5·3%)	2 (2·9%)
Slight	7 (18·4%)	5 (7·1%)
Moderate	12 (31·6%)	23 (32·9%)
Severe	8 (21·1%)	24 (34·3%)
Extreme	9 (23·7%)	16 (22·9%)
No Fatigue or Slight Fatigue	9 (23·7%)	7 (10·0%)
Moderate, Severe, or Extreme Fatigue	29 (76·3%)	63 (90·0%)
6-month		
Participants with available data	28 (73·7%)	55 (78·6%)
No tiredness/fatigue	2 (7·1%)	0 (0·0%)
Slight	3 (10·7%)	5 (9·1%)
Moderate	13 (46·4%)	19 (34·6%)
Severe	5 (17·9%)	19 (34·6%)
Extreme	5 (17·9%)	12 (21·8%)
No Fatigue or Slight Fatigue	5 (17·9%)	5 (9·1%)
Moderate, Severe, or Extreme Fatigue	23 (82·1%)	50 (90·9%)
12-month		
Participants with available data	21 (55·3%)	52 (74·3%)
No tiredness/fatigue	2/21 (9·5%)	1/52 (1·9%)
Slight	2/21 (9·5%)	3/52 (5·8%)
Moderate	9/21 (42·9%)	19/52 (36·5%)
Severe	7/21 (33·3%)	16/52 (30·8%)
Extreme	1/21 (4·8%)	13/52 (25·0%)
No Fatigue or Slight Fatigue	4 (19·0%)	4 (7·7%)
Moderate, Severe, or Extreme Fatigue	17 (81·0%)	48 (92·3%)
Confidence in the diagnosis, mean (SD)		
Baseline	7·4 (2·6)	8·3 (2·4)
Participants with available data	38 (100%)	68 (97·1%)
6-months	6·0 (2·8)	7·2 (3·0)
Participants with available data	25 (65·8%)	49 (70·0%)
12-months	7·3 (2·7)	7·2 (2·6)
Participants with available data	20 (52·6%)	49 (70·0%)
Revised Illness Perception Questionnaire, mean (SD)		
Identity Baseline	8·9 (2·9)	9·1 (2·1)
Participants with available data	38 (100%)	68 (97·1%)
Identity 6-months	9·3 (3·2)	9·8 (2·7)
Participants with available data	25 (65·8%)	49 (70·0%)
Identity 12-months	8·0 (3·8)	9·6 (2·9)
Participants with available data	19 (50·0%)	50 (71·4%)
Causes Baseline	40·1 (10·9)	40·6 (11·9)
Participants with available data	37 (97·4%)	70 (100%)
Causes 6-months	43·3 (8·9)	39·1 (10·8)
Participants with available data	25 (65·8%)	48 (68·6%)
Causes 12-months	42·6 (10·7)	40·7 (10·9)
Participants with available data	19 (50·0%)	50 (71·4%)
Timeline Baseline	22·7 (5·3)	21·4 (4·6)

Participants with available data	38 (100%)	70 (100%)
Timeline 6-months	22·9 (5·0)	22·0 (4·7)
Participants with available data	25 (65·8%)	49 (70·0%)
Timeline 12-months	22·6 (5·4)	22·3 (3·9)
Participants with available data	20 (52·6%)	50 (71·4%)
Timeline cyclical Baseline	14·1 (3·8)	13·9 (4·1)
Participants with available data	38 (100%)	70 (100%)
Timeline cyclical 6-months	13·5 (3·3)	13·4 (3·7)
Participants with available data	25 (65·8%)	49 (70·0%)
Timeline cyclical 12-months	13·6 (3·3)	13·4 (3·5)
Participants with available data	19 (50·0%)	50 (71·4%)
Consequences Baseline	24·2 (4·8)	24·4 (3·9)
Participants with available data	38 (100%)	70 (100%)
Consequences 6-months	23·0 (4·9)	23·3 (4·4)
Participants with available data	25 (65·8%)	49 (70·0%)
Consequences 12-months	21·8 (5·5)	23·5 (4·4)
Participants with available data	19 (50·0%)	49 (70·0%)
Personal control Baseline	17·3 (3·5)	18·4 (4·1)
Participants with available data	38 (100%)	70 (100%)
Personal control 6-months	18·2 (3·7)	19·1 (3·3)
Participants with available data	25 (65·8%)	49 (70·0%)
Personal control 12-months	18·8 (4·5)	18·3 (3·7)
Participants with available data	20 (52·6%)	50 (71·4%)
Treatment control Baseline	15·2 (2·7)	16·5 (3·3)
Participants with available data	38 (100%)	70 (100%)
Treatment control 6-months	16·1 (2·7)	16·0 (2·7)
Participants with available data	25 (65·8%)	49 (70·0%)
Treatment control 12-months	16·2 (3·4)	15·2 (2·9)
Participants with available data	19 (50·0%)	50 (71·4%)
Illness coherence Baseline	13·3 (5·1)	13·9 (4·9)
Participants with available data	38 (100%)	70 (100%)
Illness coherence 6-months	14·4 (5·3)	15·2 (5·0)
Participants with available data	25 (65·8%)	49 (70·0%)
Illness coherence 12-months	15·0 (5·7)	16·0 (5·3)
Participants with available data	20 (52·6%)	50 (71·4%)
Emotional representation Baseline	22·4 (5·9)	21·4 (5·9)
Participants with available data	38 (100%)	69 (98·6%)
Emotional representation 6-months	21·7 (4·6)	20·4 (6·6)
Participants with available data	25 (65·8%)	49 (70·0%)
Emotional representation 12-months	19·2 (5·7)	20·4 (5·5)
Participants with available data	20 (52·6%)	50 (71·4%)
TOTAL Baseline	175·2 (21·4)	176·3 (20·9)
Participants with available data	37 (97·4%)	67 (95·7%)
TOTAL 6-months	179·3 (16·1)	175·1 (18·6)
Participants with available data	25 (65·8%)	48 (68·6%)
TOTAL 12-months	175·1 (20·1)	176·5 (18·9)
Participants with available data	19 (50·0%)	49 (70·0%)

Extended Patient Health Questionnaire, mean (SD)		
Assessed at baseline only	17·6 (6·2)	17·7 (5·7)
Participants with available data	38 (100%)	68 (97·1%)

25. Results: Sensitivity Analyses

Compliance

Among the 141 participants who received intervention in COVID groups A, B and D, 8 participants had missing values in the number of sessions attended, which is less than 10% (8/141=5·7%) of the participants in the intervention group. The number of sessions attended within these participants is summarised as follows:

Supplementary table 25.1

Number of sessions	n/N	%
0	2/133	1·5
3	1/133	0·8
6	3/133	2·3
7	3/133	2·3
8	12/133	9·0
9	111/133	83·5
14	1/133	0·8

Based on the statistical analysis plan, participants who have been offered and could participate in at least five sessions in the intervention group will be deemed as being compliers. The number and proportion of compliers among participants who received intervention in COVID groups A, B and D is summarised as follows:

Supplementary table 25.2

Complier		Non-complier		Missing values	
n/N	%	n/N	%	n/N	%
130/133	97·7	3/133	2·3	8/141	5·7

Among 141 participants in Groups A, B and D included in the main primary and secondary analyses, there were 130 compliers (92·2%), 3 non-compliers (2·1%) and 3 participants with missing compliance value (5·7%). Due to a high proportion of compliance and a relatively low proportion of missing compliance values, we decided to not conduct a Complier Average Causal Effect (CACE) sensitivity analysis.

Missing Data

Among the 247 participants in COVID groups A, B and D, there were 6 (2·4%) participants with missing data and 241 (97·6%) participants without any missing data.

Due to a low proportion of missing data in the primary outcomes (2·4%), we decided to note conduct the analysis to examine the effect of missing data.

The Effect of COVID-19

There are 247 (73·5%) participants in COVID groups A, B and D and 89 (26·5%) participants in COVID group C. Adding a supplementary fixed effect of group indicator and its interaction with the assigned treatment to the primary analysis model, we did not find that the intervention differs by COVID group indicator (COVID group C vs A, B and D) (p=0·825):

Supplementary table 25.3

Variable	Estimate	95% CI
Randomisation group	3·268	[-2·691, 9·227]
COVID indicator	-3·662	[-11·286, 3·961]
Interaction term	1·507	[-11·848, 14·861]

Supplementary table 25.4 Physical Functioning at 12 months

COVID groups	N	Estimate	95% CI
A, B, C and D	314	4·294	[-0·848, 9·437]
A and B	151	4·863	[-2·508, 12·234]
D	83	0·354	[-8·550, 9·257]

Dose response analysis

We added an interaction term between the number of sessions attended and the intervention on the primary analysis model. The number of sessions attended for the 106 participants in the control group is set to be 0. Among the 141 participants in the intervention group, 8 participants had missing values in the number of sessions attended, which is less than 10% (8/141=5·7%) of the participants in the intervention group. We found that those in COVID groups A, B and D attended more sessions in the treatment groups differed in their 12-month SF36 PF (p=0·037):

Supplementary table 25.5

	N	Estimate	95% CI
SF36 Physical Function	236	3·047	[0·177, 5·917]

26. Adverse Events

Supplementary table 26.1 Investigator-reported adverse events: These events were entered into the trial database by the research team or the participants clinical team.

	COVID Groups A, B and D		COVID Groups C and X*	
	Specialist Physiotherapy	**Treatment as usual**	**Specialist Physiotherapy**	**Treatment as usual**
Participants with at least 1 event	41 (29·1%)	26 (24·5%)	6 (15·8%)	9 (12·9%)
Total number of events	64	32	9	13
Severity				
Mild	35	12	4	6
Moderate	18	15	4	7
Severe	11	5	1	0
Intervention Action				
None	58	30	7	12
Temporally Interrupted	6	2	2	1
Outcome				
Resolved	39	18	5	10
Resolved with sequelae	8	1	2	0
Not resolved	17	13	2	3
Relationship to intervention				
Not related	56	32	9	13
Possibly	1	0	0	0
Probably	6	0	0	0
Definitely	1	0	0	0

*COVID Group X, were those who were unassigned to a COVID group as they were lost to follow-up at the time the COVID groups were assigned, or they had withdrawn from the study.

Supplementary table 26.2 Patient-reported adverse events: These events were reported by participants in their 6- and 12-month follow-ups. The events were not vetted by the research team and there was cross-over with the investigator reported adverse events.

	COVID Groups A, B and D		COVID Groups C and X[a]	
	Specialist Physiotherapy	**Treatment as usual**	**Specialist Physiotherapy**	**Treatment as usual**
Participants with at least 1 event	59 (41·8%)	48 (45·3%)	9 (23·7%)	16 (22·8%)
Total number of events	95	71	15	29
Is this a new problem or worsening of an old problem?				
New	56	38	9	16
Old	39	33	6	13
Is the problem ongoing?				
Yes	81	57	13	24
No	14	14	2	4
Unspecified	0	0	0	1
Did this problem require a hospital admission?				
Yes[b]	8	10	0	2
No	87	61	15	26
Unspecified	0	0	0	1
Did you go to the hospital accident and emergency (casualty)?				
Yes	14	19	2	4
No	81	52	13	24
Unspecified	0	0	0	1
Did you see your GP for this problem?				
Yes	58	45	9	22
No	35	26	6	6
Unspecified	2	0	0	1
Because of this problem, have you taken time off work?				
Yes	17	17	3	8
No	78	54	12	20
Unspecified	0	0	0	1

[a]COVID Group X, were those who were unassigned to a COVID group as they were lost to follow-up at the time the COVID groups were assigned, or they had withdrawn from the study.
[b]These events were also recorded as serious adverse events (hospitalisation qualifies as serious)

27. Serious Adverse Events

A serious adverse event was defined as any untoward occurrence that results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or consists of a congenital anomaly or birth defect, or is otherwise considered medically significant by the investigator.[6]

Supplementary table 27.1 Serious Adverse Events

	COVID Groups A, B and D		COVID Groups C and X*	
	Specialist physiotherapy	**Treatment as usual**	**Specialist physiotherapy**	**Treatment as usual**
Participants with at least 1 event	24 (17·0%)	18 (17·0%)	4 (10·6%)	9 (12·8%)
Total events reported	35	24	9	10
Total number of deaths	1	0	0	0

*COVID Group X, were those who were unassigned to a COVID group as they were lost to follow-up at the time the COVID groups were assigned, or they had withdrawn from the study.

All serious adverse events were assessed by the Trial Management Group and the independent Data Monitoring and Ethics Committee, and all were classified as unrelated to treatment.

One event resulted in death, which was death by suicide of a participant receiving specialist physiotherapy. The medical notes for this case were recalled, examined and it was concluded that a possible relationship was unlikely as there were other clear risk factors directly associated with the event. Remaining events qualified as serious due to hospitalisation.

In post hoc analysis, we considered safety from the perspective of a deterioration in the primary outcome, as defined by a 10-point reduction in the SF-36 Physical Functioning domain at 12-months compared to baseline. In the specialist physiotherapy group, 16 (12%) reported a 10-point reduction, compared to 18 (17%) in treatment as usual.

Supplementary table 27.2 Classification of serious adverse events

Classification was based on the presenting symptoms and may not necessarily reflect the true aetiology of the event. For example, participants admitted to hospital with chest pain, may have had panic and/or anxiety contributing to their symptoms.

All COVID Groups (A,B,C,D)	**Number of events**	**Number of participants**	**Severity**	**Number of events in specialist physiotherapy / treatment as usual**
Gastroenterology	16	13	Severe n=2 Moderate n=5 Mild n=8	10/6
Neurology	15	13	Moderate n=10 Mild n=5	5/10
Respiratory	9	8	Moderate n=9	5/4
Cardiology	7	6	Severe n=2 Moderate n=4 Mild n=1	4/3
Urology	6	6	Moderate n=4 Mild n=2	2/4
Oncology	6	1	Severe n=5 Moderate n=1	1/0
Gynaecology	5	4	Moderate n=3 Mild n=1	2/3
Psychiatry	5	4	Severe n=4 Mild n=1	3/2

Orthopaedics	3	3	Moderate n=1 Mild n=2	2/1
Haematology	2	2	Moderate n=2	2/0
Dermatology	1	1	Mild n=1	1/0
ENT	1	1	Mild n=1	1/0
Maxillofacial	1	1	Moderate n=1	0/1
Unknown	1	1	Unknown	1/0

28. Potential Diagnostic Reclassifications

If a trial participant reported an adverse event, serious adverse event, or any other clinical event that may have indicated that a new diagnosis had been made that could account for the participant's neurological symptoms, we investigated to consider if the original diagnosis of FMD should be revised.

Diagnostic revisions were categorised according to the categories described by Stone et al, 2009. See over the page for the full list of diagnostic revision categories. For each potential case, the participant's neurologist was asked to review the medical notes, consider if the diagnosis should be revised, and assign a diagnostic revision category. The diagnostic revisions were reviewed by the Trial Management Group and the independent Data Monitoring and Ethics Committee.

Summarised details of each case are presented below, with some details withheld to preserve the anonymity of the participants. In summary, 10 potential diagnostic revisions were investigated (5 from specialist physiotherapy, 5 treatment as usual), with the resulting classifications:

- No change to diagnosis: 4 cases
- Comorbid diagnostic change: 2 cases
- De novo development of disease: 2 cases
- Prodromal diagnostic change: 1 case
- Diagnostic error: 1 change

Supplementary table 28.1 Diagnostic revisions

	Group	Description of event	Revision category
1	TAU	Incidental finding of small ischaemic lesion on head MRI, performed for other purposes and unrelated to the presenting neurological symptoms.	De novo development of new disease
2	SP	On a background of weakness diagnosed as FMD, the participant started to experience new limb tremor. A dopamine transporter scan was reported as borderline, and there was clinical uncertainty as to whether they had Parkinson's disease. The participant continued to have positive signs of functional weakness. The neurologist concluded that the participant may have subtle emerging signs of Parkinson's disease, in which case the functional weakness, which predated the tremor by 12-18 months may be occurring as a prodrome symptom.	Prodromal diagnostic change
3	SP	A new diagnosis of Benign paroxysmal positional vertigo (BPPV). It was considered unlikely that this was present at the onset of the symptoms diagnosed as FMD as there was no evidence of this from the history or examination as documented. The symptoms described by the participant at baseline could not be explained by BPPV.	De novo development of new disease
4	TAU	The participant reported experiencing new symptoms and that they were being investigated for a possible new diagnosis (the specific differential diagnosis is not specified here to preserve anonymity). Based on the description of symptoms, age of onset and past medical history, the differential diagnosis was considered unlikely. The new symptoms were consistent with the diagnosis of functional neurological disorder.	No change
5	SP	Worsening cognitive function was investigated by a neurologist specialising in memory disorders. On the basis of neuropsychological assessments, the neurologist concluded that the cognitive symptoms were functional in nature or related to depression.	No change

6	TAU	The participant reported being admitted to hospital with a suspected transient ischaemic attack (TIA). Imaging showed no signs of cerebrovascular disease. The discharge summary did not report a new diagnosis of stroke or TIA. The presenting symptoms were consistent with functional neurological disorder.	No change
7	SP	During the study period the participant experienced a seizure and was diagnosed with epilepsy. The participant had a historical diagnosis of seizures associated with a period of illness. The diagnosis of epilepsy could not explain the presenting motor symptoms.	Comorbid diagnostic change
8	TAU	The participant received a new diagnosis of a degenerative neurological disease (not specified here to preserve anonymity). Due to the relative proximity of the new diagnosis and recruitment into the trial, the original diagnosis of FMD was considered a diagnostic error, rather than being classified as a prodromal diagnostic change.	Diagnostic error
9	SP	An incidental finding on MRI was investigated and considered unrelated and unable to explain the participant's motor symptoms.	No change
10	TAU	The participant underwent a neurosurgical procedure for a pre-existing structural lesion. The lesion was considered unlikely to account for the participants presenting symptoms and the surgical procedure did not lead to improvement in the symptoms.	Comorbid diagnostic change

Key: TAU=Treatment as usual; SP=Specialist physiotherapy

Supplementary table 28.2 Diagnostic Revision Categories

Stone J, Carson A, Duncan R, et al. (2009) Brain 132, 2878–2888. https://doi.org/10.1093/brain/awp220[7]

Type of diagnostic revision		Example
0.	No change	No new neurological events or diagnoses have occurred. For example, a patient with a diagnosis of functional tremor presents to A&E with sudden onset left sided weakness. The discharge diagnosis was "possible stroke" but after further review of investigations the most likely diagnosis was acute onset functional weakness.
1	Diagnostic error	Patient presented with symptoms that were plausibly due to multiple sclerosis. The diagnosis of multiple sclerosis had not been considered and was unexpected at follow-up.
2	Differential diagnostic change	Patient presented with symptoms that were plausibly related to a number of conditions. Doctor suggested chronic fatigue syndrome as most likely but considered multiple sclerosis as a possible diagnosis. Appropriate investigations and follow-up confirmed multiple sclerosis.
3	Diagnostic refinement	Doctor diagnosed epilepsy but at follow-up the diagnosis is refined to juvenile myoclonic epilepsy.
4	Comorbid diagnostic change	Doctor correctly identified the presence of both epilepsy and non-epileptic seizures in the same patient. At follow-up, one of the disorders has remitted.
5	Prodromal diagnostic change	Patient presented with an anxiety state. At follow-up the patient has developed a dementia. With hindsight, anxiety was a prodromal symptom of dementia but the diagnosis could not have been made at the initial consultation as the dementia symptoms (or findings on examination or investigation) had not developed.
6	*De novo* development of organic disease	Patient is correctly diagnosed with chronic fatigue syndrome. During the period of follow-up, the patient develops subarachnoid haemorrhage as a completely new condition.
7	Disagreement between doctors—without new information at follow-up	Patient is diagnosed at baseline with chronic fatigue syndrome and at follow-up with chronic Lyme disease by a different doctor even though there is no new information. However, if the two doctors had both met the patient at follow-up, they would still have arrived at the same diagnoses. This would be reflected in similar divided opinion among their peers.
8	Disagreement between doctors—with new information at follow-up	Patient is diagnosed at baseline with chronic fatigue syndrome and at follow-up with fatigue due to a Chiari malformation by a different doctor because of new information at follow-up, (in this case an MRI scan ordered at the time of the first appointment). However, the first doctor seeing the patient again at follow-up continues to diagnose chronic fatigue syndrome believing the Chiari malformation to be an incidental finding. This would be reflected in divided opinion among their peers.

29. Author Group

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Gillian	Szeto
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