Specialist physiotherapy for functional motor disorder in England and Scotland (Physio4FMD): a pragmatic, multicentre, phase 3 randomised controlled trial

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Summary

Background Functional motor disorder—the motor variant of functional neurological disorder—is a disabling condition that is commonly associated with poor health outcomes. Pathophysiological models have inspired new treatment approaches such as specialist physiotherapy, although evidence from large randomised controlled trials is absent. We aimed to assess the clinical effectiveness of a specialist physiotherapy intervention for functional motor disorder compared with treatment as usual.

Methods In this pragmatic, multicentre, phase 3 randomised controlled trial at 11 hospitals in England and Scotland, adults with a clinically definite diagnosis of functional motor disorder, diagnosed by a neurologist, were included. Participants were randomly assigned (1:1, stratified by site) using a remote web-based application to either specialist physiotherapy (a protocolised intervention of nine sessions plus follow-up) or treatment as usual (referral to local community neurological physiotherapy). Individuals working on data collection and analysis were masked to treatment allocation. The primary outcome was the physical functioning domain of the 36-item short form health questionnaire (SF36) at 12 months after randomisation. The primary analysis followed a modified intention-to-treat principle, using a complete case approach; participants who were unable to receive their randomised treatment due to the suspension of health-care services during the COVID-19 pandemic were excluded from the primary analysis. This trial is registered with the International Standard Randomised Controlled Trial registry, ISRCTN56136713, and is completed.

Findings Recruitment occurred between Oct 19, 2018, and March 11, 2020, pausing during the COVID-19 lockdown, and resuming from Aug 3, 2021, to Jan 31, 2022. Of 355 participants who were enrolled, 179 were randomly assigned to specialist physiotherapy and 176 to treatment as usual. 89 participants were excluded from the primary analysis due to COVID-19 interruption to treatment (27 were assigned to specialist physiotherapy and 62 to treatment as usual). After accounting for withdrawals (n=11) and loss to follow-up (n=14), the primary analysis included data from 241 participants (138 [91%] assigned specialist physiotherapy and 103 [90%] assigned treatment as usual). Physical functioning, as assessed by SF36, did not differ significantly between groups (adjusted mean difference 3·5, 95% CI −2·3 to 9·3; p=0·23). There were no serious adverse events related to the trial interventions. 35 serious adverse events were recorded in the specialist physiotherapy group by 24 participants (17·0%), and 24 serious adverse events were recorded in the treatment as usual group by 18 participants (17·0%); one death occurred in the specialist physiotherapy group (cause of death was recorded as suicide). All were considered unrelated to specialist physiotherapy.

Interpretation Although more participants who were assigned specialist physiotherapy self-rated their motor symptoms as improved and had better scores on subjective measures of mental health, the intervention did not result in better self-reported physical functioning at 12 months. Both the specialist and community neurological physiotherapy appeared to be a safe and a valued treatment for selected patients with functional motor disorder. Future research should continue to refine interventions for people with functional motor disorder and develop evidence-based methods to guide treatment triage decisions.

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Introduction

Functional neurological disorder is a common presentation in neurological services.[1] Currently, there is consensus that the disorder can be diagnosed accurately, is disabling, and often has a poor outcome if left untreated.[2–4] Treatment is most often thought of in terms of psychotherapeutic input, but physical rehabilitation has emerged as a promising intervention for the motor

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See Online for appendix

Research in context

Evidence before this study

We searched Ovid MEDLINE from database inception to May 9, 2023, with the terms ("functional neurological", "functional movement", "psychogenic", "conversion", "hysterical", "hysteria", "non-organic", "nonorganic", "functional neurological symptom disorder", "dissociative neurological symptom disorder", or "Conversion Disorder/") AND ("physiotherapy", "physical therapy", "rehabilitation", "exercise", "Physical Therapy Modalities/" or "Neurological Rehabilitation/") AND ("Randomized Controlled Trial/", "Cohort Studies/", or "Case Reports"). We did additional searches using Google Scholar and hand searched reference lists. We identified 15 case studies, 36 cohort studies (with between three and 305 participants), and three randomised controlled trials. One randomised trial compared hypnosis and multidisciplinary rehabilitation with multidisciplinary rehabilitation alone. The other two trials compared physical therapy with a control: the first had a cross-over design and compared 3 weeks of inpatient multidisciplinary rehabilitation for functional gait disorder with a 4-week waitlist control, after which the control group crossed over to receive the intervention; the second trial was a feasibility study for the current trial. In both studies, ratings of physical health, but not mental health, were maintained with the intervention at 6 months. Despite promising outcomes from physical-based interventions for functional motor disorder, adequately powered randomised controlled trials are sparse, and data beyond 6 months' follow-up are needed.

Added value of this study

To the best of our knowledge, Physio4FMD is the first fully powered randomised controlled trial of a physical therapy-based intervention for functional motor disorder and is the largest randomised study of people with functional motor disorder published to date. The intervention followed a treatment protocol and was described in a way that allows it to be replicated and refined by others. We have also shown that large randomised trials of a complex intervention involving people with functional motor disorder can be delivered with high compliance and retention.

Implications of all the available evidence

In this trial, we found no difference between specialist physiotherapy and treatment as usual on the physical functioning domain of the 36-item short form health questionnaire at 12 months. Participants in the specialist physiotherapy group were more likely to rate their motor symptoms as improved, compared with those assigned to treatment as usual, and measures of mental health were also rated as improved. The results also suggest that physiotherapy is safe when patients are selected for treatment and physiotherapists are supported by experienced clinicians. However, the frequency of serious adverse events unrelated to physiotherapy was high, reflecting the complex nature of this patient population, the existence of multimorbidity, and the need for multidisciplinary support. Taken together with all the available evidence, physiotherapy appears to be a valuable treatment for selected people with functional motor disorder.

symptoms of functional neurological disorder.[5] Contemporary approaches to the diagnosis of functional neurological disorder rely on clinical signs, such as Hoover's sign for functional weakness, that highlight differences between impaired voluntary movement and preserved automatic movement.[6] Advances in diagnosis, along with new pathophysiological models have led to progress being made in specialist physiotherapy interventions.

We developed a specialist physiotherapy protocol for treatment of the motor symptoms of functional neurological disorder, which we refer to here as functional motor disorder. The intervention was informed by a Bayesian model of functional neurological disorder,[7] and aims to target the individual's expectations and excessive body-focused attention. Both expectation and attention are presumed to be key mechanisms driving symptoms.[8] The protocol builds on expert consensus recommendations for physiotherapy for functional motor disorder[9] and was tested with promising outcomes in a prospective cohort study and a randomised feasibility study.[10,11] In the feasibility study,[11] 60 people with functional motor disorder were randomly assigned either the specialist physiotherapy protocol, comprising nine sessions conducted over 5 consecutive days, or treatment as usual, defined as referral to community neurological physiotherapy. At 6 months' follow-up, 72% of participants in the specialist physiotherapy group rated their symptoms as improved on a 5-point scale, compared to 18% of those receiving treatment as usual. A range of physical outcome measures showed a moderate to large difference in favour of specialist physiotherapy.

In this Article, we report the findings of Physio4FMD, which is a phase 3 randomised trial based on the feasibility study. The primary aim was to identify the clinical effectiveness of specialist physiotherapy compared with treatment as usual for people with functional motor disorder at 12 months after random assignment, with a 6-month interim assessment.

Methods

Study design

Physio4FMD is a pragmatic, multicentre, phase 3 randomised controlled trial comparing a specialist physiotherapy programme for functional motor disorder with treatment as usual. The study was conducted in the UK National Health Service (NHS) at 11 secondary and tertiary care hospitals in England and Scotland. Ethics approval was granted by the London–Surrey Borders Research Ethics Committee, reference number

18/LO/0486, on March 28, 2018. The trial was registered with the International Standard Randomised Controlled Trial registry, ISRCTN56136713. The study protocol has been published previously (appendix p 3).[12] The conduct of the trial was monitored by an independent trial steering committee (which included expert clinicians, a statistician, a health economist, and patient representatives), and an independent data monitoring and ethics committee.

Participants

Study participants were adults (aged ≥18 years) attending outpatient neurology clinics and inpatients who had a diagnosis of functional motor disorder (ie, they could be both new and returning patients). Eligibility for participation was assessed by consultant neurologists collaborating in the trial, who made the clinically definite diagnosis of functional motor disorder, according to the Gupta and Lang diagnostic classification criteria.[13] Further inclusion criteria were that diagnostic investigations had been completed, the individual was accepting of receiving the trial interventions, and motor symptoms were causing substantial distress or impairment in social, occupational, or other important areas of functioning (subjectively described by the individual), independent of other comorbidities (ie, the distress or impairment should be attributable to functional motor disorder rather than other co-existing health problems). All participants had to provide written informed consent.

If the recruiting neurologist deemed the individual to have severe psychiatric comorbidity, which would interfere with their ability to participate in physiotherapy, they were not considered for inclusion in the study. Moreover, we excluded anyone who had another diagnosis that could account for the majority of the symptoms or disability; had pain, fatigue, or dissociative seizures that would interfere with their ability to engage with physiotherapy; had disability to the extent that they require assistance for toileting; was unable to attend nine sessions of physiotherapy over a 3-week period, within 6 weeks of their initial neurology consultation; had an ongoing unresolved compensation claim or litigation; had no fixed address or was seeking rehousing through their council for disability access reasons; did not have sufficient English comprehension to complete questionnaires; had a documented learning disability that prevented them from answering questionnaires independently; and did not have capacity to give consent. Eligibility was ultimately a clinical decision made by the neurologist, rather than by cut-off scores from standardised assessment tools. Individuals were not excluded on the basis of pain, fatigue, dissociative seizures, anxiety, or depression. These symptoms were only considered as exclusionary if they were deemed to be severe enough to interfere with the patients' ability to engage with the physiotherapy intervention. Sex data were reported by participants with options of female or male.

Randomisation and masking

After completing the baseline assessment, participants were randomly assigned (1:1) to specialist physiotherapy or treatment as usual by the trial manager at St George's University of London (London, UK). Randomisation was done using a web-based application created by an independent company, Sealed Envelope. Block randomisation was done with random block sizes to ensure even allocation between randomised groups, stratified by site. The randomisation sequence was computer generated and programmed by an independent statistician. Researchers collecting the trial outcomes, statisticians, and health economists were masked to treatment allocation, and participants were asked not to reveal their group allocation to research workers. Due to the nature of the intervention, it was not possible to mask the trial manager, participants, or treating clinicians.

For more on **Sealed Envelope** see https://www.sealedenvelope.com/

Procedures

At an initial consultation, before enrolment in the trial, the diagnosis of functional motor disorder was made by a neurologist based on best practice recommendations,[3] and according to diagnostic criteria.[13] A follow-up neurology consultation was to be held within 12 months of the initial consultation. Individuals meeting eligibility criteria were asked if they consented to be contacted about the study by a research worker. A face-to-face appointment with a member of the research team was held with consenting individuals, during which a second screening for eligibility was done, informed consent was obtained, and baseline assessments were completed before random assignment (appendix pp 8–15). The study neurologists received training from MJE, JS, or GN to standardise the way functional motor disorder and the study was explained to participants (appendix pp 4, 8).

The intervention was a protocolised specialist physiotherapy programme that could be adapted to the different needs of individuals, as described elsewhere.[9–12] The programme consisted of nine sessions delivered within a 3-week period, plus a single follow-up session 3 months after the sessions ended. The intervention had three broad aims: to help patients understand their symptoms; to retrain movement with redirection of attention away from focusing on their body; and to develop self-management skills. Physiotherapy sessions were guided by an interactive workbook,[14] which formed part of the self-management plan. The physiotherapists delivering the intervention were specialised in neurorehabilitation. Before the trial, all physiotherapists had completed a 5-day training programme supported by an intervention manual (appendix p 16).[15]

The comparator condition was treatment as usual, defined as a referral made by the diagnosing neurologist to the NHS community neurological physiotherapy

service. A referral letter was sent with the neurology consultation letter, which stated the diagnosis of functional motor disorder and that the patient might benefit from physiotherapy. As there is no formal pathway or guideline for functional motor disorder treatment in the NHS, we were aware that the treatment received by this group would be of mixed quality. Due to the pragmatic nature of the trial, we were unable to control whether physiotherapy was received or how many sessions were offered to those allocated to this group.

Follow-up assessments for both groups were done remotely at 6 months and 12 months via the participants' preferred method (either an online form, return-mail paper forms, or by telephone). A questionnaire to assess fidelity and satisfaction with treatment was conducted by the trial manager or a designated (unblinded) research worker via telephone, between 6 and 12 months after randomisation.

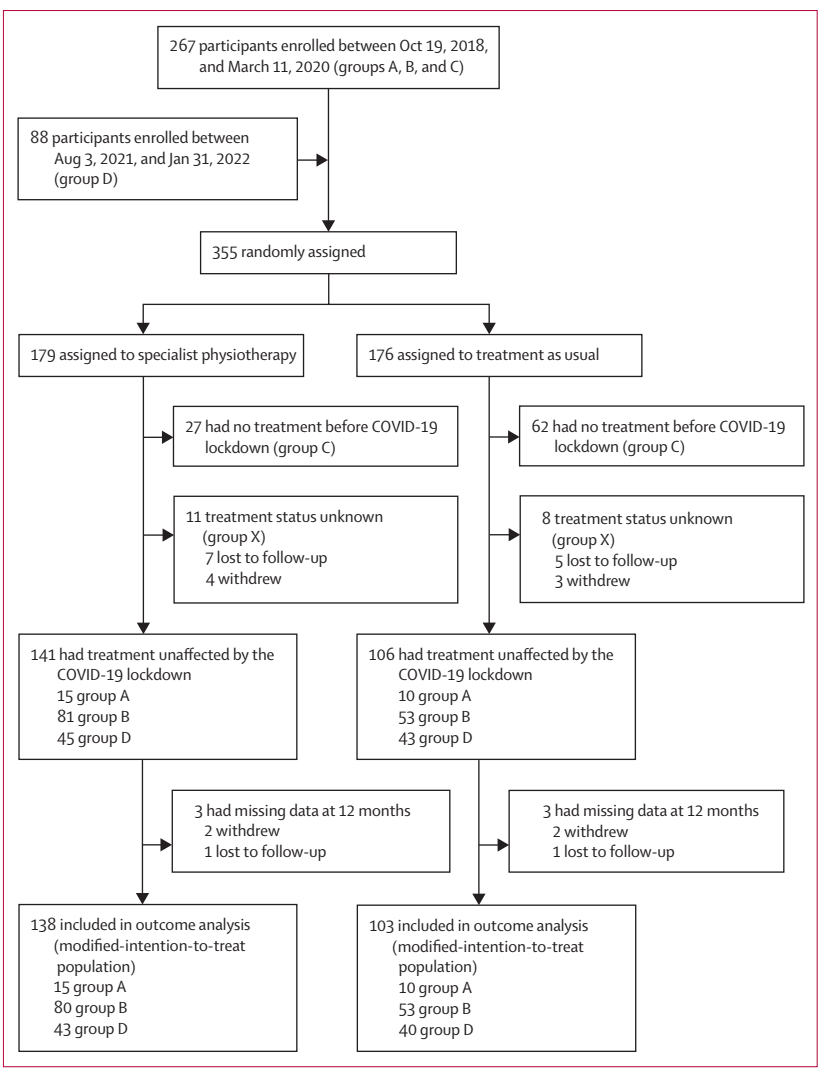

Figure 1: **Trial profile**
Group A completed treatment and follow-up before March 23, 2020 (when national COVID-19 lockdown was instigated in the UK). Group B completed treatment before March 23, 2020, but completed follow-up after March 23, 2020. Group C were randomly assigned to treatment groups but did not receive treatment before March 23, 2020, and therefore completed follow-up after March 23, 2020. Only 30 (34%) participants in group C received their physiotherapy treatment within the trial follow-up period (eight from specialist physiotherapy, received at a median of 253 days post randomisation; 22 from treatment as usual, received at a median of 174 days post randomisation). Group D were recruited in the extension period from Aug 3, 2021. Group X did not have treatment status established, withdrew, or were lost to follow-up before 12 months. At the 6-month interim analysis, 134 people assigned specialist physiotherapy and 97 assigned treatment as usual were included.

Outcomes

The primary outcome was the physical functioning domain of the patient-reported 36-item short form health questionnaire (SF36) at 12 months after randomisation.[16] The physical functioning domain includes ten questions for participants to self-rate their degree of limitation when attempting vigorous activities (eg, running or lifting heavy objects), moderate activities (eg, moving a table or pushing a vacuum cleaner), carrying groceries, climbing stairs, walking various distances, washing, and dressing. Scores range from 0 to 100, with the maximum score of 100 indicating optimal physical function.

Several secondary outcome measures of clinical effectiveness were used. The clinical global impression of improvement scale (CGI-I) is measured on a 5-point Likert scale; participants rate their perception of improvement in answer to the question, "After physiotherapy, the problem with my movement is…" with the responses either "much improved", "improved", "no change", "worse", or "much worse" (appendix p 17).[17] The remaining seven domains of the SF36 were assessed on scales of 0–100; these domains measure physical role limitations, bodily pain, general health perceptions, energy and vitality, social functioning, emotional role limitations, and mental health.[18] The functional mobility scale measures assistance needed over three distances (5 m, 50 m, and 500 m); each distance is rated from 1 to 6, with a score of 1 meaning the person uses a wheelchair and a score of 6 meaning the person has independent mobility.[19] The revised illness perception questionnaire (IPQ-R)[20] comprises subscales for identity, causes, timeline, timeline cyclical, consequences, personal control, treatment control, illness coherence, and emotional representation; total scores range from 56 to 294, with higher scores representing a higher level of perceived illness. Scores on the Hospital Anxiety and Depression Scale[21] range from 0 to 21, with scores of 8 or higher having acceptable sensitivity and specificity for cases of anxiety and depression.[22] Fatigue was self-rated on a 5-point scale as either no, slight, moderate, severe, or extreme fatigue (appendix p 18).[23] Confidence in correctness of the diagnosis of functional motor disorder was rated on a 10-point scale, with a score of 10 representing extremely confident (appendix p 19).[24] Health-care use was assessed using digital data held by NHS England and NHS Scotland on hospital-based appointments and admissions.[25,26] The Extended Patient Health Questionnaire was completed at baseline only for secondary exploratory analysis purposes (appendix p 20).[27,28] A health economic analysis was also done and will be reported separately.

All outcome measures were collected and analysed at 6 months and 12 months. Safety and adverse event data were collected as part of the self-reported 6-month and 12-month questionnaires, during the assessment of fidelity telephone call, and in follow-up clinical appointments.[29] Adverse events were defined as any untoward medical occurrence, regardless of causal relationship with treatment, that did not meet the criteria for a serious adverse event. Serious adverse events were defined as any untoward occurrence that resulted in death, was life-threatening, required hospitalisation or extension of existing hospitalisation, resulted in persistent or substantial disability or incapacity, a congenital anomaly or birth defect, or an event that was otherwise considered medically significant by the investigator. We also investigated any event that potentially indicated a new neurological diagnosis, or an incorrect original diagnosis of functional motor disorder.

Statistical analysis

The target sample size was calculated using ANCOVA to detect a 9-point difference in SF36 physical functioning with 90% power at a significance level of 5%.[12] Assuming a standard deviation of 22 and inflating the sample by a factor of 1·4 to account for therapist effect, we calculated that a minimum of 105 participants were needed per group. The target sample size was increased by 20% to account for dropouts, giving a target sample size of 132 per group. Additional participants were recruited in an extension of the trial to mitigate the effects of the COVID-19 pandemic; COVID-19 mitigation strategies were based on published guidance (appendix pp 21–22).[30–33] The study analysis plan was prespecified and published before database lock;[33] this plan details the mitigation strategies and corresponding sensitivity analyses to explore the effects of COVID-19 mitigation.[33]

Analyses were done using Stata version 18. Data were analysed following a modified intention-to-treat principle, using a complete case approach (ie, participants who were unable to receive their randomised treatment due to the suspension of health-care services during the COVID-19 pandemic were excluded from the primary analysis). The primary outcome was analysed using linear mixed effects modelling to produce adjusted mean differences, with the physiotherapist and clusters of one in the treatment as usual group as the random effect, controlling for baseline values and adjusting for site. Secondary outcomes with continuous scales were analysed using linear mixed models, adjusting for baseline values and site and standardising by baseline values of each outcome due to differences in scale. The 5-point CGI-I was dichotomised for analysis into two categories: improved ("much improved" or "improved") and not improved ("no change", "worse", or "much worse"). The 5-point fatigue scale was similarly dichotomised into "no fatigue", "slight fatigue", or "moderate fatigue" and "severe fatigue" or "extreme fatigue". The dichotomised scores were analysed using mixed effects logistic regression, adjusting for baseline values for fatigue and site using fixed effects. Digital data for hospital appointments or admissions were analysed using mixed effects negative binomial regression.

Proportions, means, and SDs are reported for self-reported health-care usage. No adjustments were made for multiple testing. If substantial data were missing, predictors of missingness would be added to the models.

	Specialist physiotherapy (n=141)	Treatment as usual (n=106)
Age, years		
Mean (SD)	45·0 (14·3)	44·4 (14·9)
Median (IQR)	48 (33–55)	45 (31–55)
Gender		
Male	37 (26%)	27 (26%)
Female	104 (74%)	79 (75%)
Ethnicity		
White	126 (89%)	97 (92%)
Black	6 (4%)	1 (1%)
Asian	6 (4%)	2 (2%)
Mixed	2 (1%)	5 (5%)
Other	1 (<1%)	1 (1%)
Relationship status and dependants		
Married or cohabitating with partner	77 (55%)	63 (59%)
Single, separated, or widowed	64 (45%)	43 (41%)
Has dependants	52 (37%)	41 (39%)
Care needs		
Has a carer (paid or unpaid)	56 (40%)	27 (26%)
Has a paid carer	17 (12%)	7 (7%)
Education		
No qualification	11 (8%)	4 (4%)
General Certificate of Secondary Education	35 (25%)	25 (24%)
A level	25 (18%)	16 (15%)
National Vocational Qualification	26 (18%)	17 (16%)
Higher National Certificate or Diploma	16 (11%)	7 (7%)
Degree	18 (13%)	27 (26%)
Higher Degree	9 (6%)	9 (9%)
Other	1 (<1%)	1 (1%)
Years of education, mean (SD)	14·2 (3·8)	14·4 (2·8)
Employment status		
Working or studying	49 (35%)	37 (35%)
Not working or studying because of sickness	40 (28%)	31 (29%)
Not working because of unemployment	42 (30%)	29 (27%)
Other	10 (7%)	9 (9%)
Previous treatment		
Physiotherapy	69/139 (50%)	42/104 (40%)
Psychology	25/139 (18%)	17/104 (16%)
Occupational therapy	22/139 (16%)	8/104 (8%)
Specialist inpatient rehabilitation	5/137 (4%)	4/104 (4%)
Symptom duration, years		
Mean (SD)	5·2 (7·2)	4·4 (4·9)
Median (IQR)	2·6 (1·3–6·0)	2·6 (1·1–5·4)

(Table 1 continues on next page)

	Specialist physiotherapy (n=141)	Treatment as usual (n=106)
(Continued from previous page)		
Dominant motor symptom		
Weakness	47 (33%)	31 (29%)
Gait disturbance	45 (32%)	35 (33%)
Tremor	21 (15%)	13 (12%)
Mixed movement disorder	19 (14%)	16 (15%)
Jerks	7 (5%)	6 (6%)
Dystonia or fixed dystonia	2 (1%)	5 (5%)
Body part affected*		
Left upper limb	68 (48%)	43 (41%)
Right upper limb	68 (48%)	45 (43%)
Left lower limb	99 (70%)	74 (70%)
Right lower limb	92 (65%)	75 (71%)
Head or neck	36 (26%)	20 (19%)
Trunk	31 (22%)	13 (12%)
Dominant hand		
Right	128 (91%)	97 (92%)
Left	13 (9%)	9 (9%)

Data are n (%) unless otherwise specified. Percents might not sum to 100 due to rounding. Group A (n=25) completed follow-up before March 23, 2020 (when national COVID-19 lockdown was instigated in the UK). Group B (n=134) completed treatment before March 23, 2020, but completed follow-up after March 23, 2020. Group D (n=88) were recruited in the extension period from Aug 3, 2021. *Participants could select more than one option.

Table 1: **Baseline characteristics of participants who received allocated treatment (groups A, B, and D)**

If only few data were missing, analyses would be conducted as complete case.

Prespecified sensitivity analyses were also done to explore the effect of COVID-19 on the trial, the effect of the COVID-19 mitigation strategies, and a treatment–response analysis for therapy sessions (appendix pp 21–22).[33] Intervention compliance was also explored as a pre-specified analysis: in the case of low compliance, Complier Average Causal Effect was planned; in the case of high compliance, descriptive statistics were planned. High compliance was defined as attending five or more sessions of specialist physiotherapy.[33]

In a post-hoc analysis, participants who made a clinically significant improvement in the primary outcome was examined. The minimum clinically important difference for the SF36 has been found to differ by population studied and this value has not been established in functional motor disorder; we therefore chose a conservative value of 10 points of difference, based on other conditions.[34]

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Recruitment occurred over 24 months in two blocks: from Oct 19, 2018, to March 11, 2020, and from Aug 3, 2021, to Jan 31, 2022, with a 17-month break during the COVID-19 pandemic. Due to the nature of the recruitment method, we were unable to collect data for the number of people screened for inclusion. 355 participants were randomly assigned to specialist physiotherapy (n=179) or treatment as usual (n=176) during the two recruitment periods (figure 1).

Participants were categorised into four groups (designated A, B, C, and D) based on the effect of the COVID-19 pandemic on their treatment. Participants in groups A, B, and C were all enrolled during the first recruitment block, and those in group D were enrolled during the second block (figure 1). Group A participants completed treatment and follow-up before March 23, 2020 (when national COVID-19 lockdown was instigated in the UK). Group B participants completed treatment before March 23, 2020, but completed follow-up after March 23, 2020. Group C participants were randomly assigned to treatment groups but did not receive treatment before March 23, 2020, and therefore completed follow-up after March 23, 2020. Only 30 (34%) participants in group C received their physiotherapy treatment within the trial follow-up period (eight from specialist physiotherapy, received at a median of 253 days after randomisation; 22 from treatment as usual, received at a median of 174 days post randomisation). Group D participants were recruited in the extension period from Aug 3, 2021.

Participants in group C (n=89) were excluded from primary and secondary outcome analyses because the COVID-19 lockdown delayed their treatment and prevented most from receiving their allocated treatment before the 12-month analysis. Group C contained more participants from the treatment as usual group (n=62) compared with specialist physiotherapy (n=27) due to longer waits to start treatment after participants were randomised. These participants were included for both sensitivity and safety analyses. 19 participants recruited in the first block could not have their treatment status established and were excluded from primary and secondary outcome analyses also; these people were designated as group X for safety analyses only (figure 1). Therefore, 247 participants from groups A (n=25), B (n=134), and D (n=88) had treatment unaffected by the COVID-19 lockdown (figure 1). Table 1 presents baseline data for participants in groups A, B, and D, of whom 141 were assigned specialist physiotherapy and 106 were assigned treatment as usual. Mean age was 44·7 years (SD 14·6), 183 (74%) were female and 64 (26%) were male, and the mean symptom duration was 4·8 years (SD 6·3). Baseline data for participants who were in groups C and X are in the appendix (pp 23–24). Data for past medical history of all participants are in the appendix (pp 25–29).

An additional six participants (three in each group) had missing data (due to withdrawal or loss to follow-up) at the 12-month assessment; therefore data for primary and secondary outcome analyses were available for 138 (91%)

	Specialist physiotherapy			Treatment as usual			Mean difference, adjusted for baseline (95% CI)
	Baseline	12 months	Change from baseline at 12 months	Baseline	12 months	Change from baseline at 12 months	
SF36 physical functioning (primary outcome)	26·3 (23·1)	37·1 (28·4)	10·7 (25·0)	30·9 (23·2)	37·2 (28·5)	5·9 (22·7)	3·5 (–2·3 to 9·3)
Participants with available data	141 (93%)	138 (91%)	..	106 (93%)	103 (90%)	..	..
SF36 physical role limitations	20·9 (21·3)	33·0 (26·9)	12·0 (27·1)	21·9 (22·2)	31·8 (27·0)	10·0 (23·5)	2·3 (–3·7 to 8·2)
Participants with available data	141 (93%)	138 (91%)	..	106 (93%)	103 (90%)	..	..
SF36 bodily pain	28·4 (22·7)	35·4 (26·4)	6·8 (20·8)	32·6 (23·3)	37·1 (25·6)	4·6 (23·1)	1·1 (–4·6 to 6·9)
Participants with available data	141 (93%)	138 (91%)	..	106 (93%)	103 (90%)	..	..
SF36 general health perceptions	34·2 (19·4)	34·9 (18·9)	1·3 (15·7)	37·1 (21·7)	35·5 (20·9)	–1·7 (17·8)	1·8 (–2·0 to 5·6)
Participants with available data	141 (93%)	136 (89%)	..	106 (93%)	103 (90%)	..	..
SF36 energy and vitality	22·2 (16·7)	29·8 (20·3)	7·5 (19·4)	22·3 (18·0)	26·1 (18·7)	3·2 (18·1)	3·8 (–0·9 to 8·4)
Participants with available data	141 (93%)	137 (90%)	..	106 (93%)	103 (90%)	..	..
SF36 social functioning	29·5 (22·6)	38·8 (27·7)	9·2 (28·9)	30·8 (26·5)	38·1 (27·5)	7·6 (28·8)	1·1 (–5·4 to 7·5)
Participants with available data	141 (93%)	137 (90%)	..	106 (93%)	103 (90%)	..	..
SF36 emotional role limitations	48·7 (34·3)	51·1 (32·0)	2·1 (30·8)	50·8 (36·8)	48·9 (33·5)	–1·6 (30·5)	3·7 (–2·9 to 10·1)
Participants with available data	141 (93%)	138 (91%)	..	106 (93%)	103 (90%)	..	..
SF36 mental health	52·3 (21·5)	55·1 (23·3)	2·4 (18·8)	54·0 (21·7)	51·4 (23·9)	–2·8 (19·0)	5·4 (0·9 to 9·8)
Participants with available data	141 (93%)	137 (90%)	..	106 (93%)	103 (90%)	..	..
Functional mobility scale	11·4 (4·5)	12·2 (4·5)	0·8 (3·2)	11·5 (4·4)	11·9 (4·6)	0·3 (3·4)	0·6 (–0·2 to 1·4)
Participants with available data	140 (92%)	136 (89%)	..	104 (91%)	97 (85%)	..	..
Hospital Anxiety and Depression Scale—anxiety	10·3 (5·0)	10·0 (5·2)	–0·2 (3·9)	9·5 (5·2)	9·4 (4·9)	0·4 (3·4)	–0·5 (–1·4 to 0·4)
Participants with available data	140 (92%)	135 (89%)	..	105 (92%)	97 (85%)	..	..
Hospital Anxiety and Depression Scale—depression	8·8 (4·1)	8·5 (4·7)	–0·2 (3·8)	8·3 (4·4)	8·2 (4·8)	0·1 (3·7)	–0·2 (–1·2 to 0·8)
Participants with available data	140 (92%)	135 (89%)	..	105 (92%)	97 (85%)	..	..
Fatigue							
No, slight or moderate fatigue	83 (59%)	67 (49%)	..	53 (50%)	48 (49%)	..	1·1 (0·6 to 2·0)*
Severe, or extreme fatigue	58 (41%)	69 (51%)	..	53 (50%)	49 (51%)	..	..
Participants with available data	141 (93%)	136 (89%)	..	106 (93%)	97 (85%)	..	..
Confidence in the diagnosis	8·1 (2·0)	8·1 (2·3)	0·0 (2·5)	8·0 (2·2)	7·4 (2·8)	–0·7 (2·5)	0·8 (0·2 to 1·4)
Participants with available data	141 (93%)	134 (88%)	..	106 (93%)	94 (82%)	..	..
Revised illness perception questionnaire (total score)	176·0 (16·8)	178·0 (17·9)	3·0 (15·0)	175·5 (21·6)	176·2 (19·5)	3·5 (13·6)	0·2 (–3·4 to 3·8)
Participants with available data	133 (87%)	129 (85%)	..	102 (89%)	94 (82%)	..	..

Data are mean (SD) or number (%), unless otherwise stated. SF36 subtype scores range from 0 to 100, with a maximum score of 100 indicating optimal health. Scores on the functional mobility scale range from 3 to 18, with a minimum score of 3 meaning the person uses a wheelchair and a maximum score of 18 meaning the person has independent mobility. Hospital Anxiety and Depression Scale scores range from 0 to 21, with a score ≥8 indicating anxiety or depression. Fatigue is measured on a five-point scale (no, slight, moderate, severe, and extreme). Confidence in the diagnosis is measure on a scale from 0 to 10, with a score of 0 meaning not at all confident and a score of 10 meaning extremely confident. Revised illness perception questionnaire total scores range from 56 to 294; appendix pp 49–51). Data for the secondary outcome of clinical global impression of improvement are reported in figure 3. SF36=short form 36 questionnaire. *Odds ratio for no, slight or moderate fatigue compared with severe or extreme fatigue at 12 months; due to insufficient degrees of freedom in the final data, site was removed from the final model for the 5-point fatigue scale.

Table 2: **Primary and secondary outcome data (groups A, B, and D)**

of 152 (groups A–D, X) participants assigned specialist physiotherapy and 103 (90%) of 114 assigned treatment as usual (figure 1). These participants comprised the modified intention-to-treat population; those with missing data were excluded. The primary outcome—self-rated physical functioning on SF36—did not differ between treatment groups at 12 months (adjusted mean difference 3·5, 95% CI –2·3 to 9·3, p=0·23; intraclass correlation coefficient for specialist physiotherapy was 0·095, 95% CI 0·00–0·25, table 2). For secondary outcomes at 12 months, 81 (59%) individuals assigned specialist physiotherapy rated their symptoms on the CGI-I as "much improved" or "improved", compared with 39 (38%) who were assigned treatment as usual (odds ratio [OR] 2·3, 95% CI 1·4–3·9; figure 2). No differences between groups on other domains of the SF36 were seen, although a nominal improvement on the mental health domain was noted for specialist physiotherapy compared with treatment as usual (figure 3). No differences between groups were noted on the functional mobility scale, for anxiety or depression (as assessed by the Hospital Anxiety and Depression Scale), or for fatigue (table 2, figure 3; appendix pp 42–51). For the IPQ-R total score, no difference between groups was noted; when the subscales were assessed separately (appendix p 49–51), personal control and illness

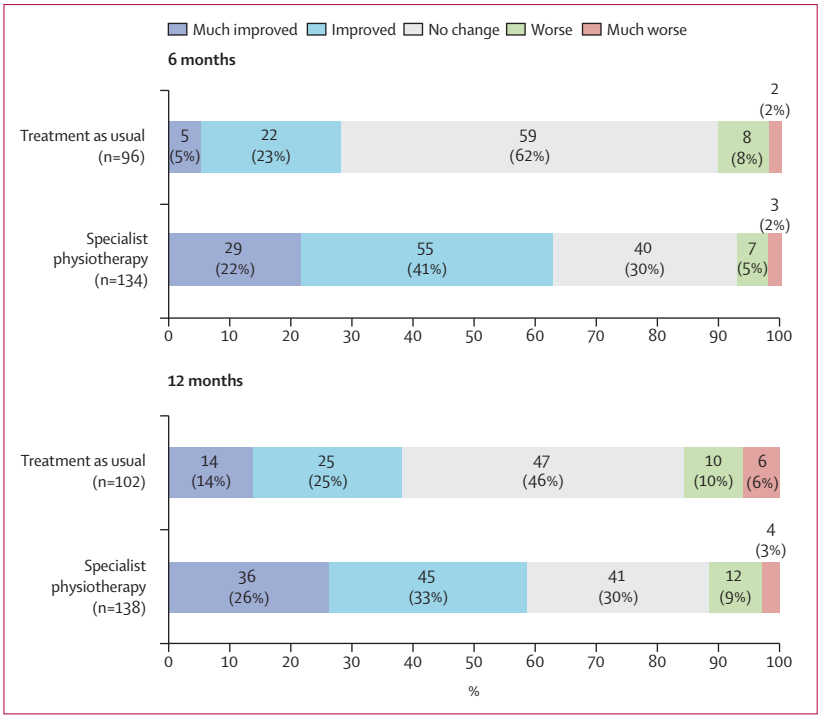

Figure 2: **Clinical global impression of improvement at 6 months and 12 months (secondary outcome)**
The odds ratio for improvement with specialist physiotherapy compared with treatment as usual was 4·7 (95% CI 2·6–8·6) at 6 months and 2·3 (1·4–3·9) at 12 months.

coherence scores seemed to nominally favour specialist physiotherapy. Confidence in the diagnosis was nominally greater with specialist physiotherapy (table 2, figure 3; appendix pp 52–56). No differences were found between groups for NHS digital data on hospital appointments and admissions (appendix p 46).

The median time between randomisation and commencing treatment was 36 days (IQR 24·8–57·8) for specialist physiotherapy and was 97 days (60·2–176·2) for treatment as usual. The median duration of treatment (days between first and final treatment session) was 15 days for specialist physiotherapy (10·0–21·5) and 93 days (47·0–148·5) for treatment as usual. The median time between completing treatment and completing the primary outcome (physical functioning domain of the SF36 at 12 months) was 310 days (281·5–323·0) for specialist physiotherapy and 179 days (123·0–237·5) for treatment as usual. The median number of treatment sessions completed was 9 (8–9) in the specialist physiotherapy group and 4 (2–7) in treatment as usual (appendix pp 30, 36).

All randomly assigned participants with follow-up data were included in sensitivity analyses (n=315; 158 in the specialist physiotherapy group and 157 in the treatment as usual group). There was 89% (315 of 355) retention for the primary outcome. 130 (92%) of 141 individuals were compliant with the specialist physiotherapy intervention (defined as attending five or more sessions). Sensitivity analyses revealed that including participants from group C in the analysis had no effect on the primary outcome. When analysing data from all randomly assigned participants, the adjusted mean difference between groups was 4·3 (95% CI –0·8 to 9·4), which is not significant but does favour specialised physiotherapy (appendix pp 57–58). The treatment–response analysis suggested that attending more sessions was associated with better scores for the primary outcome. However, due to the high compliance in this study, this finding is a nominal one as only nine participants attended less than eight sessions. Due to high levels of compliance and low levels of missing data, the pre-planned analyses to explore the effects of compliance and missing data on the results for the primary outcome were not required. High intervention compliance meant that only descriptive statistics were done. Low missing data meant that only complete analyses were done. In a post-hoc analysis, the number of participants who made a clinically significant improvement in the primary outcome (designated as a 10-point improvement) was 67 (49%) of 138 in the specialist physiotherapy group compared with 39 (38%) of 103 in the treatment as usual group.

In total, 59 serious adverse events were reported by groups A, B, and D (table 3). One event was death by suicide of a participant receiving specialist physiotherapy. The medical notes for this individual were recalled and examined, and it was concluded that a possible relation with the intervention was unlikely because other risk factors directly associated with the event were present. All serious adverse events were classified as unrelated to treatment, although possible relationships cannot be completely ruled out (appendix pp 59–62). One instance of diagnostic error was identified, resulting in a misdiagnosis rate of less than 1% at 12 months (appendix pp 63–65).

Data suggested high ratings of intervention fidelity among participants receiving specialist physiotherapy (appendix pp 31–41). Compared with treatment as usual, participants receiving specialist physiotherapy were more satisfied with their treatment; 119 (97%) of 123 participants in specialist physiotherapy were completely satisfied or satisfied compared with 49 (65%) of 75 for treatment as usual. Participants receiving specialist physiotherapy rated their physiotherapists as having a greater understanding of their movement problem than participants receiving treatment as usual (median score out of 10 was 10 *vs* 8).

Discussion

This study is, to the best of our knowledge, the first, powered, randomised controlled trial of physical rehabilitation for functional motor disorder. No difference between treatment groups was recorded for the primary outcome of physical functioning on SF36. Participants allocated to specialist physiotherapy were twice as likely to self-report an improvement in their motor symptoms at 12 months and to score their mental

health on SF36 as improved at 12 months, although these findings are nominal. The specialist physiotherapy group also self-reported having more confidence that their diagnosis was correct. With the caveat that participants were screened for their suitability for physiotherapy by expert neurologists, physiotherapy proved safe, with no serious adverse events related to treatment. The one death that was reported in the specialist physiotherapy group was judged not related to the intervention after case note review.

81 (59%) of the 138 individuals allocated to specialist physiotherapy rated their motor symptoms as improved or much improved at 12 months, and 67 (49%) of the participants in this group self-reported a 10-point improvement (designated by us as a clinically significant improvement) in the SF36 physical functioning score at 12 months from baseline. Conversely, in the treatment as usual group, 39 (38%) of 102 individuals rated their motor symptoms as improved, and the same proportion self-reported a 10-point improvement in SF36 physical functioning. The heightened perception of improvement in physical functioning by participants assigned to specialist physiotherapy could simply be a consequence of the self-rated improvement in motor functioning, but it might also be partly because these participants felt they had improved understanding of symptoms, greater perception of control over symptoms, more confidence in the correctness of the diagnosis, and higher scores on SF36 mental health compared with those allocated to treatment as usual. Altogether, these subjective changes are likely to reflect greater self-efficacy and a reduced threat of symptoms, leading to a greater perception of improvement.

Outcome measurement is notoriously difficult in functional motor disorder, with challenges including symptom heterogeneity, variability of symptom severity, and multifactorial causes of disability and distress.[35] These factors affect the validity of assessment tools and their sensitivity to change. The disparity between findings on the SF36 physical functioning domain and the CGI-I raises questions about their value as outcome measures for functional motor disorder. A 2020 international expert consensus recommendation for a core outcome measure set for functional neurological disorder recommended the CGI-I as the most useful measure, due to its resistance to symptom variability and heterogeneity.[36] With this measure, we found a difference between treatment groups in favour of specialist physiotherapy. However, validated objective outcome measures for functional motor disorder are not currently available.[36] Measures such as the simplified functional movement disorders rating scale[37] rely on the subjective assessment of a third-party observer, and thus are not objective. Although this measure would have added a valuable dimension of data to our study, its use was beyond the practical limits of this pragmatic trial. In lieu of other practicable objective measures, we included digital health-use data as a proxy measure of change, with which we did not find any significant differences.

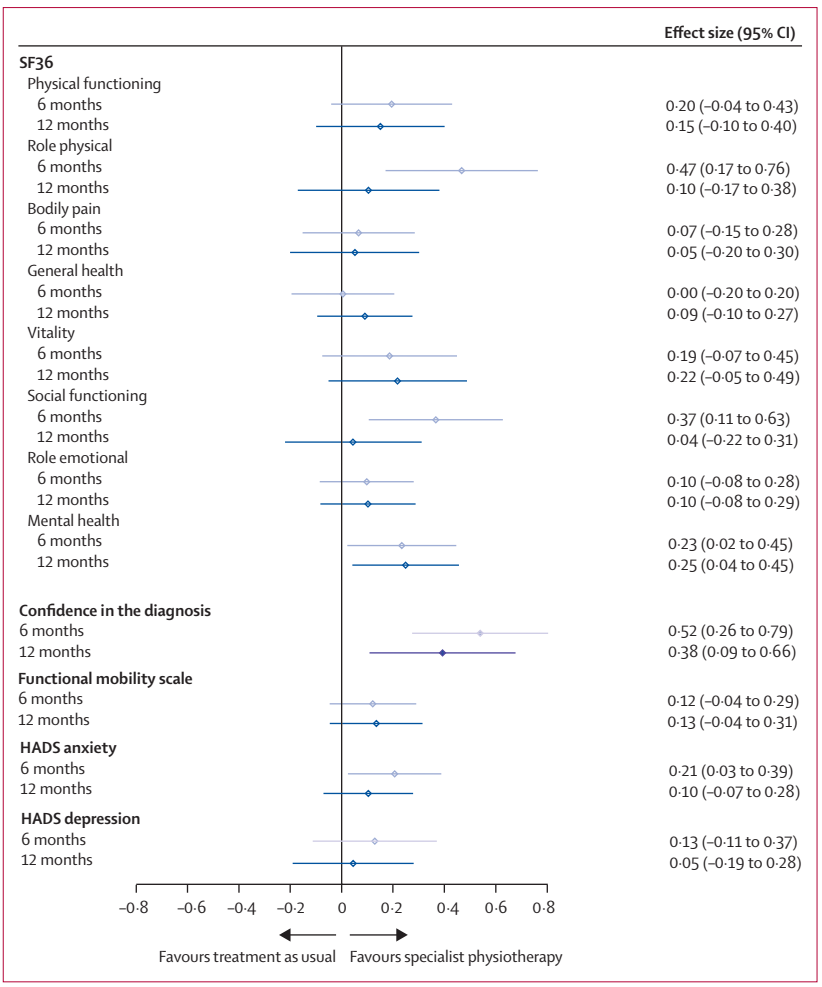

Figure 3: **Effect sizes for continuous outcome measures at 6 months and 12 months**
Data are adjusted for baseline values and sites and standardised by baseline values of each outcome due to differences in scale. HADS=Hospital Anxiety Depression Scale. SF36=Short Form 36.

The results for the primary outcome differ from those of the feasibility study, in which a moderate to large treatment effect was seen at 6 months for SF36 physical functioning.[11] However, the CGI-I outcomes are more closely aligned with the feasibility study. In the current study, improvement on the CGI-I at 6 months (defined as self-reporting "much improved" or "improved") was noted in 63% of individuals receiving specialist physiotherapy and 28% of those receiving treatment as usual (figure 2); in the feasibility study these values were 72% and 18%, respectively. The improved performance of treatment as usual in the current study compared with the feasibility study is notable and might partly account for the low difference between randomised groups. The quality of community physiotherapy in the NHS could have improved in the 5 years since the feasibility study was done, due to increased awareness, published clinical resources for physiotherapists, international conferences,

	COVID-19 groups A, B, and D		COVID-19 groups C and X	
	Specialist physiotherapy	Treatment as usual	Specialist physiotherapy	Treatment as usual
Adverse events				
Participants with at least one event	41/141 (29%)	26/106 (25%)	6/38 (16%)	9/70 (13%)
Total number of events	64	32	9	13
Relationship to treatment				
Not related	56/64 (88%)	32/32 (100%)	9/9 (100%)	13/13 (100%)
Possibly	1/64 (2%)	0/32	0/9	0/13
Probably	6/64 (9%)	0/32	0/9	0/13
Definitely	1/64 (2%)	0/32	0/9	0/13
Serious adverse events				
Participants with at least one event	24/141 (17%)	18/106 (17%)	4/38 (11%)	9/70 (13%)
Total events reported	35	24	9	10
Total number of deaths	1	0	0	0

Data are n/N (%). Group A completed follow-up before March 23, 2020 (when national COVID-19 lockdown was instigated in the UK). Group B completed treatment before March 23, 2020, but completed follow-up after March 23, 2020. Group C were randomly assigned to treatment groups but did not receive treatment before March 23, 2020, and completed follow-up after March 23, 2020. Only 30 (34%) participants in group C received their physiotherapy treatment within the trial follow-up period and the treatment was delayed (8 from specialist physiotherapy, received at a median of 253 days post randomisation; 22 from treatment as usual, received at a median of 174 days post randomisation). Group D were recruited in the extension period from Aug 3, 2021. Group X comprised participants who were lost to follow-up or who withdrew from the study.

Table 3: **Adverse events**

and the founding of an international society for functional neurological disorder.[6] This hypothesis is supported by data from the fidelity interview, which found that most participants in the treatment as usual group received treatments that were in line with consensus recommendations.[9] The improved SF36 physical functioning domain scores in both groups from baseline to 12 months also supports this argument; although some of this improvement could be explained by regression towards the mean.

Another factor in the current study that might account for the differences in findings with the feasibility study is that participants had higher SF36 physical functioning and mental health scores at baseline, suggesting high levels of physical disability, anxiety, and depression. Furthermore, the intervention was delivered more intensely in the feasibility study (nine sessions delivered consecutively over 5 days) compared with the present study (nine sessions delivered over a 3-week period), which might be associated with greater effectiveness. Differences in therapist skill and practice in delivering the intervention across the two studies also might have affected the efficacy of the intervention.

The only other published randomised trial of rehabilitation for functional motor disorder (to our knowledge) was from 2014 and compared 3 weeks of inpatient multidisciplinary treatment for functional gait disorder to a waiting list control (ie, no treatment).[38] The study found an immediate treatment effect of 8·4 units on the functional mobility scale and 11·7 units on the short form 12 (SF12) physical score, which was maintained and slightly improved at 12 months' follow-up (14·1 units). Direct comparisons with our study are limited by differences in study design and the patient cohort (ie, participants had gait disorder in the 2014 study *vs* mixed motor symptoms in the present study; and mean symptom duration was 9·5 months *vs* 4·8 years). However, both studies reported similar levels of improvement from baseline to 12 months in physical function, assuming that the SF36 physical functioning domain and SF12 physical score are comparable.

We acknowledge that this study has limitations. First, by chance, randomisation might have disadvantaged the specialist physiotherapy group, because mean symptom duration was longer compared with treatment as usual (5·2 years *vs* 4·4 years), and previous physiotherapy and occupational therapy were more frequent in the specialist therapy group, which might have meant these individuals benefited less from additional treatment. Conversely, the lower mean number of treatment sessions in the treatment as usual group and lower satisfaction with treatment favoured specialist physiotherapy. Second, with multiple secondary outcomes, significance might have occurred by chance, and we did not correct for multiple comparisons. Third, most of our outcome measures were participant reported rather than assessed by a clinician. Fourth, we designed a pragmatic trial with a real-world comparator and, therefore, did not attempt to control the treatment received by this group. The resulting treatment will have varied in terms of content, quality, duration, and waiting time. Longer waiting times for treatment as usual meant that these participants will have had concluded their treatment much closer to the 6-month and 12-month assessment points compared with individuals in the specialist physiotherapy group who will have completed treatment much further from the assessment times, which might have influenced the results (ie, the effect of specialist physiotherapy needed to last longer). Fifth, sensitivity analyses did not show differences in the primary outcome when participants who were recruited before and after the COVID-19 pandemic were assessed together, although it is impossible to rule out potential confounding factors of the treatment interruptions caused by COVID-19 lockdowns or our mitigating strategies. Sixth, we cannot rule out placebo and the effects of participants' expectations associated with the randomised groups. We attempted to minimise these non-specific effects in the way the trial was described to potential participants (appendix pp 4, 8).

Our study has several strengths, including the large sample size, a high rate of compliance and retention, follow-up over 12 months, and masking of those involved with data collection and analysis. Generalisability is supported in that the intervention was carried out at multiple sites, with high fidelity, following training and support with supervision.

Several questions remain for future research. For example, do interventions delivered earlier in the

trajectory of functional motor disorder improve outcomes? And what are the optimal components, duration, and intensity for physiotherapy? In view of the heterogeneity of the individuals with functional motor disorder, research should identify who would be most likely to benefit from specialist physiotherapy, and how we can meet the needs of those who are unlikely to benefit. More evidence is needed to guide the addition of multidisciplinary expertise to the rehabilitation of some people, such as psychological therapy and occupational therapy, and we need to consider potential adjuncts to physiotherapy, such as neuromodulation, hypnosis, and non-specific exercise. Finally, research is needed to develop validated subjective and objective outcome measures for functional motor disorder.

In conclusion, the specialist physiotherapy protocol for functional motor disorder did not result in better self-reported physical functioning compared with treatment as usual (ie, community neurological physiotherapy). Both treatment groups showed improved mean physical functioning scores over the 12-month study period. However, participants in the specialist physiotherapy group were more likely to self-rate their motor symptoms as improved. These changes occurred despite baseline assessments revealing prolonged symptom duration and high levels of physical disability, anxiety, and depression in the specialist physiotherapy group. Taken together, the subjective improvements in symptom ratings along with the very high levels of satisfaction with treatment, suggest that specialist physiotherapy could be a valued and safe treatment option for some people with functional motor disorder.

Contributors

GN led the study and wrote the first draft of the manuscript. GN, AC, MJE, LHG, RMH, JM, LM, IN, MR, and JS contributed to the study design and funding acquisition and were involved at all stages. GN and KH designed the trial intervention, wrote the intervention workbook and treatment manual, trained the physiotherapists, and provided supervision to the specialist physiotherapist group. LM and TCL designed and completed the statistical analysis. MLN was involved in the data analysis. BSS and HN were trial managers. A-MS was the lead research assistant. GN, BSS and A-MS verified the data. All authors were members of the Trial Management Group. All authors helped to interpret the data, to critically revise the manuscript for important intellectual content and approved the final version. All authors had full access to the data if desired and had final responsibility to submit the manuscript for publication.

Declaration of interests

GN receives research funding from the National Institute for Health and Care Research (NIHR); is a founding member of the Functional Neurological Disorder Society (FNDS); and is on the advisory board for FND patient charities FND Hope UK and FND Action. LM and LHG receive research funding from the NIHR. MJE does medical expert reporting in personal injury and clinical negligence cases, including in cases of functional neurological disorder; has shares in Brain & Mind, which provides neuropsychiatric and neurological rehabilitation in the independent medical sector, including in people with functional neurological disorder; has received financial support for lectures from the International Parkinson's and Movement Disorders Society and the FNDS; receives royalties from Oxford University Press for his book The Oxford Specialist Handbook of Parkinson's Disease and Other Movement Disorder; has received honoraria for medical advice to Teva Pharmaceuticals; receives grant funding, including for studies related to functional neurological disorder, from the National Institute for Health and Care Research and the Medical Research Council; is an associate editor of the European Journal of Neurology; is a member of the international executive committee of the International Parkinson's and Movement Disorders Society and a board member of the FNDS; and is on the medical advisory boards of the charities functional neurological disorder (FND) Hope UK and Dystonia UK. JS reports honoraria from UptoDate, personal fees from Expert Witness Work and grants from National Research Scotland; runs a free self-help website, www.neurosymptoms.org, for patients with Functional Neurological Disorder; and is secretary of FNDS and on the medical advisory boards of the charities FND Hope UK and FND Action. IN has received research funding from NIHR, UK Research and Innovation, and the Wellcome Trust; and was a member of a data safety and monitoring board for a RCT of herbal medication for long COVID. MR has received research funding from Epilepsy Research UK, the NIHR; receives a salary from Elsevier as Editor-in-Chief of Seizure—European Journal of Epilepsy; has received honoraria for talks on unrelated subjects from Angelini Pharma and UCB Pharma; sits on a Lennox Gastaut Syndrome advisory board for UCB Pharma; and received payment from Precisis for chairing a data safety monitoring board of an unrelated commercial study. AC receives research funding from the NIHR, the Medical Research Council, Chief Scientist Office Scotland, and European Union (Etude Program); has received an honorarium from Forum for Indian Neurological Education; personal fees from expert testimony in medicolegal cases relating to FND; is president of the FNDS; and is paid Associate Editor of the Journal of Neurology, Neurosurgery and Psychiatry. All other authors declare no competing interests.

Data sharing

Deidentified participant data can be made available by request to the corresponding author. Requests will be considered after planned analyses and reporting have been completed by the investigators. Access will require submission of a protocol that is approved by a review committee and a signed data access agreement. Due to the data sharing agreement and for patient confidentiality reasons, we are not able to provide access to hospital episode statistics data from National Health Service (NHS) England and NHS Scotland.

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