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Physical activity self-management and coaching compared to social interaction in Huntington's disease? Results from the ENGAGE-HD randomized, controlled, pilot feasibility trial

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Abstract

Background: Self-management and self-efficacy for physical activity is not routinely considered in neurologic rehabilitation.

Objective: We assessed feasibility and outcomes of a **14 week** physical activity self-management and coaching intervention compared with social contact in Huntington's disease (HD) to inform the design of a future full-scale trial.

Design: Assessor blind, multi-site, randomized pilot feasibility trial.

Setting: Participants were recruited and assessed at baseline, 16 weeks following randomisation, and then again at 26 weeks in HD specialist clinics with intervention delivery by trained coaches in the participants' homes.

Patients and Intervention: People with HD were allocated to the ENGAGE-HD physical activity coaching intervention or a social interaction intervention.

Measurements: Eligibility, recruitment, retention and intervention adherence were determined at 16 weeks. Other outcomes of interest included measures of functional, home and community mobility, self-efficacy, physical activity and disease-specific measures of motor and cognition. Fidelity and costs for both the physical activity and social comparator interventions were established.

Results: Forty % (n=46) of eligible patients were enrolled and 22 randomised to the physical intervention and 24 to social intervention. Retention rates in the physical intervention and social intervention were 77% and 92% respectively. Minimum adherence criteria were achieved by 82% of participants in the physical intervention and 100% in the social intervention. There was no indication of between group treatment effects on function, however increases in self-efficacy for exercise and self-reported levels of physical activity in the physical intervention lends support to our pre-defined intervention logic model.

Limitations: The use of self-report measures may have introduced bias.

Conclusions: An HD physical activity self-management and coaching intervention is feasible and worthy of further investigation.

Word count: 4442

Keywords: Huntington's disease; Physical Activity; Social Interaction; Randomised controlled pilot feasibility trial; health economics

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Background

Huntington's disease (HD) is a fatal, autosomal dominantly inherited neurodegenerative disorder with a prevalence of 6-13/100,000 [1]. Death usually occurs between 15 and 30 years after onset of symptoms prior to which the complex disease symptoms, including motor, cognitive and behavioral impairments, result in loss of functional independence and progressive escalation of healthcare costs[2]. The personal, social and economic consequences of HD are devastating.

Arguably in HD, to date, trials of exercise interventions have surpassed pharmacological interventions in achieving functional benefit[3–6]. Indeed numerous studies suggest that lifestyle factors, including physical activity and specific motor training, may help to drive compensatory neural networks that may in turn compensate for the failing brain and change the course of the disease[7,8]. Such interventions implemented in long term, neurodegenerative diseases such as HD have the potential to maintain function and facilitate independent living in a cost effective manner and are critical secondary prevention strategies that should be a core component of contemporary neurologic physical therapy (PT) practice. However, long term self-management skills for physical activity are rarely considered in clinical trials and home-based therapies[9].

In HD, the nature of the disease (motor and non-motor features) can negatively impact motivation to initiate and sustain participation in physical activity and exercise interventions. The associated cognitive and mood disorders such as apathy and decreased motivation can affect the willingness and the ability of individuals to engage in physical activity, structured exercise or in activities outside the home. There is little evidence for effectiveness of behavioral interventions to support longer term adherence in complicated chronic conditions including stroke[10,11] and, to our knowledge, no disease-specific approaches that have been purposely developed for HD or other highly complex neurodegenerative conditions. This is a

critical area to address not only to achieve the potential functional benefits that can be conferred from regular physical activity[12] but also to manage sedentary behaviors that place these individuals at increased risk of secondary health complications.

We aimed to assess feasibility and explore outcomes of the ENGAGE-HD physical activity self-management and coaching intervention through the conduct of a randomized, controlled, pilot feasibility trial to inform the design of a future full-scale trial[13]. In focussing on a self-management approach that encouraged autonomy and goal setting, we were also interested in understanding the relevant interactions between provider and participant. For this reason, we included a social contact comparator. We also conducted a detailed economic costing to inform our understanding of the cost-benefit relationship of a physical activity intervention in relatively-rare long term neurodegenerative diseases such as HD.

Methods

Design overview

This was a single blind, multi-site pilot feasibility trial (ISRCTN 65378754) reported in line with the CONSORT extension for randomised pilot studies [14]. Participants were assessed at baseline on enrolment into the trial. Following baseline assessment, participants were randomised to a physical activity or social interaction intervention. A blinded assessor reassessed participants at 16 weeks following randomisation, and then again at 26 weeks. At the end of the study, all participants were offered a brief version of the alternative intervention with 1 home visit and 1 follow up phone call. The schedule of enrolment, interventions, and assessments are shown in Table 1 below.

<Table 1>

Setting and Participants

The trial was conducted across eight specialist clinics in the United Kingdom (UK) with assessments conducted in the clinic (trial sites) and interventions delivered in the home environment. A full description of the trial protocol can be found elsewhere[15].

Participants were eligible if they 1) had a diagnosis of manifest HD, confirmed by genetic testing, 2) had self-reported or physician-reported difficulties with walking and/or balance (but still able to walk with minimal assistance), 3) were over 18 years old, and 4) had a stable medication regime for four weeks prior and were anticipated to maintain a stable regime for the duration. Participants were ineligible if they 1) had any physical or psychiatric condition that would prohibit the participant from completing the intervention or assessments, 2) were unable to communicate in spoken English, or 3) were involved in (or were within four weeks of completing) any other interventional trial. Enroll-HD study is an observational cohort study providing a full clinical dataset, including full medical history and medication history (https://www.enroll-hd.org/). In consenting to be enrolled in the Enroll-HD study,

participants also give their permission for their coded data to be accessed by researchers conducting other HD-related research. Participants were either required to be on Enroll-HD or the relevant medical history and data provided through participation in Enroll-HD needed to be provided independently by the site. If this data were not able to be provided by the site, participants were considered ineligible. Ethical approval was obtained at all sites and participants provided informed consent. A screening log was maintained at each site, recording numbers approached, eligible and declined.

Randomisation and blinding

Randomisation (ratio of 1:1) and automatic allocation was accomplished using a purpose developed web-based system[16]**.** Minimisation was used to achieve balance between groups based on data obtained at the baseline assessment[17]. Minimisation variables were: site of recruitment; age (< or >50 years old); gender; Unified Huntington's Disease Rating Scale (UHDRS) Total Motor Score (TMS) (< or > 45). Independent outcome assessors were blinded to group allocation. Site staff inputted the minimisation variables and this generated an allocation from an algorithm developed by our database programmers. Neither the participants nor the intervention therapists were blinded.

Interventions

Physical Activity Intervention. The Engage-HD Physical Activity intervention was grounded within the framework of self-determination theory (SDT)[18], and consisted of three main elements: the *participant/coach interaction*, the *Engage-HD Workbook* and an exercise DVD (*Move to Exercise*)[4,19]. A full description of the intervention in line with TIDieR guidelines for reporting interventions in trials[20] are published elsewhere[21] and summarised in Table 2 (contact corresponding author for additional information).

<Table 2>

Coaches conducted six home visits over 14 weeks (weeks 1, 2, 3, 6, 10 and 14) and three interim phone calls (weeks 4, 8 and 12) that served to provide encouragement in relation to regular physical activity. In partnership with their coaches, participants developed up to three realistic physical activity goals and were assisted with individual physical activity progression through goal discussion. Goal achievement was assessed by the coach at the last home visit. Exercise diaries and pedometers were provided to record the amount and type of physical activity involvement (e.g. walking or use of DVD and pedometers). Similarly, health and falls diaries facilitated documentation of falls, medication changes or contact with healthcare services.

Social Interaction Intervention. The social intervention provided conversational interaction (see Table 2). This intervention was developed by our team in order to provide us with a comparator that could help to both control for contact time and account for the potential influence of the interpersonal skills (i.e. relatedness) of the coach on any treatment effect whilst not focussing particularly on the goal setting processes inherent in a physical activity self-management intervention. This approach to facilitate the understanding of individual components of interventions is in line with the UK Medical Research Council (MRC) framework for development and evaluation of complex interventions[22].

Home visits were conducted at weeks 1, 2, 3, 6, 10 and 14 and supportive phone calls, at weeks 4, 8 and 12. At each visit, the social activity coach engaged the participant in a talking and communication interaction. Conversation cards (with images and text) representing a wide range of topics stimulated discussions (contact corresponding author for more information). Health and falls diaries were completed but we did not ask those in the social intervention to keep exercise diaries.

Coaches and training. Coaches were either a) healthcare professionals (e.g. physical therapists, occupational therapists or nurses) with experience of delivering exercise related

activities or with specific experience with HD; or b) exercise professionals. All staff had to meet specific health competencies. Nevertheless, across the sites, the coaches had a wide range of backgrounds and experiences, hence the need for centralized and standardized training and support. This was provided by the chief investigator and the intervention coordinator, both of whom were research physical therapists with extensive experience working with the HD community in both clinical practice and research. All coaches attended a 1 day face-to face training day prior to the start of the trial at each site and were trained to deliver both the physical and social interventions according to structured protocols. In addition, physical activity coaches participated in a minimum of two phone/video conferences (per participant) with the intervention coordinator to discuss goal setting or any participant-specific concerns or issues.

A coach's manual provided a session-by-session guide, familiarized the coaches with the specific challenges of working with patients with HD, and offered a background to the intervention's SDT framework. Full details of the visit schedules, training and coaching support are reported elsewhere[21].

Intervention fidelity. The multiple modalities of intervention delivery necessitated different fidelity measures. Fidelity of the physical activity intervention was measured using a combination of self-report checklists, independent analysis of audio recordings and a self-assessment completed by the intervention coaches. Full details of physical activity intervention fidelity (including the use of a purpose developed rating scale) are published elsewhere[21]**.** Social intervention fidelity was assessed as total time spent in the home during the visit and length of interim telephone calls. This was chosen to control for any confounds in relation to contact time. As a further evaluation, coaches were asked to record details of the conversations that we used to confirm the focus of discussions (and in particular to establish that the discussions were not related to physical activity).

Outcomes and Follow-up (see Table 1)

Baseline measures included age, gender, height, weight, level of education, Social Support for Exercise survey and several disease-specific measures. The Social Support for Exercise survey[23] assesses the level of support individuals feel they are receiving from family and friends while making health behavior changes. Disease specific measures (obtained from Enroll-HD or clinical records) included the Unified Huntington's Disease Rating Scale (UHDRS) [24] Total Motor Score (TMS), which measures voluntary and involuntary motor impairments specific to HD, and Total Functional Capacity (TFC), which assesses capacity to work, handle finances, perform domestic chores and self-care tasks, and live independently. Functional Assessment and Independence Scale were also assessed. Medication at baseline (coded as analgesic, anti-choreic, anti-depressant, antihypertensive, diabetes and other) was also recorded.

We defined a-priori feasibility objectives based on our evaluation of eligibility (assessed through screening logs maintained at each research site) and recruitment and retention rates (monitored through a bespoke clinical trials database and evaluated based on the final number of participants successfully consented, randomised and retained)). We also monitored completion of outcome measures, protocol deviations (using standard operating procedures as part of a formal quality management system inherent in a UK registered clinical trials unit) and documented both intervention fidelity and adherence to the intervention (measured using patient diaries) as well as safety (adverse event reporting documented in accordance with the governance requirements of safety reporting in a trial not involving an investigational medicinal product). We agreed that a retention rate greater than the 75% would suggest that the intervention and trial processes were feasible. If the proportion retained was less than this but greater than 65%, we would consider adjusting the intervention. Adherence to both the physical and social intervention was considered sufficient

if at least 75% of the participants completed visit one, two and three with their activity coach (of a possible six visits). We set this threshold for adherence relative to the number of visits required to discuss all content of the physical activity workbook and to agree goals. The minimum threshold for adherence to exercise diary completion was defined as valid data reported for at least four days or more in over half the weeks during the intervention for any one of the components.

As recommended in the CONSORT extension for randomised pilot studies [14], reporting of effect size estimates and measures of uncertainty is critical to inform fully powered future evaluation. We therefore explored a range of potential outcomes in both groups. Function was assessed using the Physical Performance Test (PPT), an assessment incorporating a series of 9 primarily timed functional tasks that are converted to categorical variables (0-4) and summed to give a score between 0 (severe problems) and 36 (minimal problems)[25]. Self-reported physical activity was measured using the International Physical Activity Questionnaire (IPAQ) – short form [26]. Home and community mobility was reflected by the Life Space Assessment[27]. The Lorig scale provided a measure of self-efficacy[28]. Walking ability was assessed using the six minute walk test[29], a measure of walking endurance that measures distance walked in 6 minutes, and the Timed up and Go Test[30], which measures the time to stand up from a chair, walk 3 meters turn and walk back, and sit down. Participants completed the EQ-5D generic health capability measure[31] and the ICECAP-A generic health measure via interview[32]. Self-reported frequency, circumstance and severity of any falls over the past four months was recorded at the baseline, primary end point assessments and over the past two months at follow up. The PAS Healthcare Climate Questionnaire (short form)[33] was used to assess participants' perceptions of the degree to which their coach accommodated their individual needs, choices and perspectives. Motor function was assessed using the modified UHDRS Motor Score (mMS), a subset of items in the UHDRS TMS,

chosen due to its specific focus on voluntary motor impairments. Cognitive function was assessed using verbal fluency and symbol digit modality tests[34], both of which have been shown to be sensitive to cognitive impairments in HD[34].

Statistical Analysis

We planned to recruit 62 participants to estimate feasibility proportions for retention and adherence within 14 percentage points either side using a 95% confidence interval. This target allowed for 25% loss to follow up. Descriptive analyses (with 95% confidence intervals where relevant) included an evaluation of eligibility, recruitment, retention rates, completion of outcome measures and assessments. Diary usage was summarised by constituent components i.e. DVD use, pedometer use and reported walking time. Falls diary data were analysed using frequency analysis.

Both unadjusted and adjusted between group differences for outcome measures are presented. Adjusted estimates were calculated controlling for baseline measures of outcome scores (i.e. Analysis of Covariance (ANCOVA)) in addition to the balancing variables (age, gender and UHDRS motor score). This approach was taken in order to provide the most valid effect size estimates for this relatively rare study population[35].

Standard transformations were explored to improve model fit. All these analyses were on an intention to treat (ITT) basis although the primary analysis used the complete case data set.

The cost to deliver both the physical and social interventions was calculated by multiplying the hourly salary rate of the intervention staff (including salary on costs) by the time taken to arrange, travel to and conduct sessions; mileage costs were based on a reimbursement rate of £0.40 per mile. Journey time and mileage was calculated as the round trip (e.g. a 12 minute journey to visit the participant is recorded as 24 minutes of staff time).

Role of the funding source: The funders had no involvement in the conduct of this pilot feasibility trial.

Results

Feasibility

Participants were recruited between 23 June 2014 and 21 August 2015. There was variability in screening processes at sites with some sites screening large numbers of potential participants, of whom a small fraction were eligible, and an even smaller fraction were recruited. Others screened only eligible participants and recruited over three quarters of those screened (see Table 3 for a summary of screening, enrolment and recruitment information according to site).

One hundred and fifteen (46%) out of 249 HD patients screened were eligible (with many of these excluded based on the recruiting clinician's impression that they had a physical or psychiatric condition that would prevent them from completing the intervention); 46 (40%) were enrolled, 22 randomised to the physical intervention and 24 to the social intervention. Only 2 of the trial sites recruited to time and target, although we did recruit 46 participants (74% of the target). It was necessary to extend the time period for recruitment by 2 months and furthermore to implement active site monitoring in some situations where recruitment was particularly slow. The main reasons for sites struggling to recruit were related to either competing drug trials (in 4 of the sites) or to research staff maternity and/or long term illness (in 2 of the sites). Of the 138 participants that were deemed ineligible 62 of these (45%) were excluded on the grounds that they had a 'physical or psychiatric condition that would prohibit the participant from completing the intervention or assessments'. This included people with advanced chorea and those known not to engage with healthcare services. Baseline characteristics were similar between groups (see Table 4 and Figure 1).

<Table 3 here>

<Figure 1>

<Table 4>

There were three full withdrawals in the physical activity group (felt unable/ did not want to complete intervention (n=2); change in home circumstances and illness (n=1)) with one withdrawal from the intervention only (due to illness), and two losses to follow up in the physical group (death (n=1); prolonged hospitalisation (n=1)) prior to the primary endpoint (see Figure 1). Two participants in the social contact group missed the primary end point assessment, but did complete the follow up assessment. This resulted in a retention rate of 77% (95% CI: 54-91%) in the physical activity group and 92% (72-99%) in the social contact group.

Intervention fidelity and adherence

Mean (SD) interaction time spent in the home for the physical activity intervention across all visits was 58.3 (8.9) minutes. Mean (SD) time spent in discussion across telephone calls was 10.1 (6.7) minutes. Mean (SD) interaction time spent in the home for the social intervention across all visits was 50.7 (2.7) minutes. Mean (SD) time spent in discussion across telephone calls was 10.7 (6.7) minutes. Median (range) number of physical activity intervention visits completed were 6 (0-6) and social activity intervention visits were 6 (3-6). In the physical intervention arm, 82% of participants completed visits one, two and three and 68% completed all scheduled visits; 100% of participants in the social intervention completed visits one, two and three and 88% completed all visits.

Exercise diary data was available for 17/22 participants at the primary endpoint (only those in the physical intervention completed the exercise diaries). Thirteen (76%) participants adhered to at least one component of the intervention for a minimum of seven weeks during the course of the intervention. Forty-six % of participants recorded walking time, 51% recorded pedometer readings and 70% recorded using the DVD. The average daily time spent using the DVD over 13 weeks was 16.4 (SD 3.0) minutes, the average daily time spent walking was 63 minutes (SD 14.5) with average daily pedometer count 6,254 steps (SD 998).

Participant goals (Physical Intervention only)

Up to three goals were recorded by the end of visit 3 for the 19 participants in the physical activity group. In total, 50 goals were recorded for 19 participants; 19 of these were related to walking, 21 to structured exercise, 6 to increasing general activity, 2 to reducing sitting time and 2 were sports and recreational activity based. Of the 19 participants that recorded goals at the start of the intervention, 3 participants (1 who had made three goals and 2 who had made two goals) did not complete the intervention. Sixty-seven % of goals were achieved at the expected outcome or better with the majority of these being related to general activity goals and walking goals.

Outcomes

Table 5 summarises the baseline and follow-up scores of key outcome variables, as well as presenting unadjusted and adjusted between group differences. Both unadjusted and adjusted differences indicate potential treatment effects for the IPAQ, Life Space, self-efficacy for exercise and symbol digit modality test, which should be explored in future confirmatory trials.

<Table 5>

Falls

During the intervention period, 16 physical activity group participants used falls diaries regularly and 14 falls were reported; 23 social activity intervention group participants used diaries regularly and 24 falls were reported.

Adverse events

In total, seven adverse and three serious adverse events (two intervention; death (n=1) & prolonged hospitalisation due to deterioration in mental health status (n=1), one social; hospitalisation due to deterioration in mental health status) were reported during the trial);

none were related to the intervention and were primarily as a result of concurrent illnesses. Two of the adverse events involved falls; one from falling on ice and one from tripping on the stairs, both of which required medical attention but not hospital admission (one physical intervention, one social arm).

Cost of Physical Intervention Delivery

Our economic analysis used 2014/15 as a cost year, and a public sector perspective of analysis. One-hundred-and-five home visits were delivered at a total cost of £5,982 (mean cost per session £56.97, SD £34.72). This equates to a cost £341.82 per participant. Mean contact time for participants in the physical intervention arm was 57.7 minutes per home session. Telephone calls cost an additional £2.77 per contact. In total, 22.8 hours *(*1370 minutes) were spent discussing the physical intervention with the lead intervention coordinator. The per participant cost of lead intervention supervision was £52.97. The costs to develop the intervention and the cost associated with training staff to deliver the intervention have been reported previously[21].

Cost of Social Intervention Delivery

For the social intervention, participants received one-hundred-and-thirty-nine visits, delivered at a total cost of £5387 (mean cost per session £38.76, SD £20.05). Mean contact time for participants in the social intervention was of 50.6 minutes per home session. Telephone calls cost an additional £2.79 per contact. Supervision time with the lead intervention coordinator for the social intervention was minimal (£3.03 per participant).

Discussion

This trial has helped to establish feasibility and explore adherence and outcomes in relation to a purpose-developed physical activity behavior change intervention for people with HD in comparison to a social contact comparator. We have shown that it is possible to recruit

participants to this study and through the robust intervention description and development of comprehensive training and monitoring of associated fidelity we have clear indications of how to support the delivery of such a trial. The dropout rate was lower in the social intervention than physical intervention. Trial discontinuation records suggest that those participants withdrawing from the physical intervention were faced with a variety of unrelated life challenges and reported difficulty in complying with the requirements of the physical activity intervention. This highlights the importance of considering the personal challenges experienced by those living with a neurodegenerative disease so that therapists are able to identify when individuals may benefit from extra support to sustain physical activity. This trial was conducted across 6 specialist centres in the UK covering both rural and urban areas. The intervention was highly manualised, included expert oversight from a lead intervention therapist and preliminary cost analyses that altogether provides excellent evidence for designing future definitive trials in a UK setting.

Critical to our intervention development was acknowledgement of the complex array of cognitive, behavioral and motor symptoms that can lead to highly risky sedentary behaviors in HD[36]. Our intervention approach included one-to-one coaching and telephone support and a coaching style that highlighted autonomy, competence and relatedness as well as considering disease specific barriers (in this case cognitive limitations and apathy, a common behavioral problem in HD) and wider environmental and social aspects. To our knowledge, this is the first implementation of a social contact comparator in a physical activity intervention trial targeting a neurological population; thus the observable between-group differences in physical activity provides **some initial suggestion** that the coaching approach was indeed linked to physical activity outcomes rather than benefit incurred through social contact. The relative increase in self-efficacy for exercise along with increased levels of physical activity as a result of the coaching intervention despite the complexity of

impairments in HD reinforces the importance of specific support for exercise in complex and chronic conditions such as HD and is therefore a target for future confirmatory studies. It also lends supports to our pre-defined logic model and gives us some confidence that the observed outcomes, namely improved lifespace and self-efficacy could be related to the intervention inputs. However, it is likely that a critical factor to achieving functional benefit is exercise adherence over a longer duration.

We must acknowledge the limitations inherent in this pilot feasibility trial. The large number of outcome measures may have been unduly burdensome for sites and participants, but we are now in a position to define a more focussed assessment battery in a definitive trial. Additionally, the self-report measures utilized, such as the IPAQ, may have introduced bias. Employing more intuitive monitoring approaches, e.g. wearable technologies to quantitatively measure physical activity[37], may be helpful. This study also did not assess any carer impact as result of the person with HD participating in this trial. Future trials may want to consider recruiting carer-companions or HD family dyads not only to optimise recruitment and retention but also to facilitate wider physical activity related health benefits[38].

Defining and developing methods to facilitate physical activity behavior change is of great interest to neurologic physical therapy practice. This may in part be due to the greater acknowledgement of the critical role for physical activity as a potential disease modifying intervention[39,40], but more likely the urgent need for implementing secondary preventive strategies for the large numbers of individuals living with a chronic diseases[41]. There is an increasing focus on the development and evaluation of theory-driven approaches embedded in specifically tailored programs to achieve sustained behaviour change for people with neurodegenerative and neuro-inflammatory diseases such as Parkinson's Disease (PD) and Multiple Sclerosis (MS)[42–48]. Here we report the first such pilot feasibility trial in HD, a well characterized single gene neurodegenerative disorder that is an excellent model that can be

easily adapted to individuals with dementias and movement disorders more generally[49], as well as for individuals with rare neurodegenerative diseases. Supporting ongoing physical activity in an environment of changing physical and cognitive function has the potential to enhance meaningful participation in usual life activities and could lead to important public health benefits for these populations. Given the success achieved (with relatively low cost) in this highly challenging and complex condition, we suggest that this approach has wider applicability and should be subject to a full scale efficacy evaluation in HD over a longer duration and is worthy of exploration in a broad range of neurodegenerative conditions where cognition, behaviour and apathy limit ongoing physical activity engagement.

Relevant conflicts of interest/financial disclosures: Nothing to report.

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Table 1: Schedule of enrolment, interventions, and assessments

STUDY PERIOD														
	Enrolment		Allocation	Post-allocation									Follow-up	
TIMEPOINT**	- 4 wks	0	0	2 wks	3 wks	4 wks	6 wks	8 wks.	10 wks	12 wks	14 wks	15 wks	16 wks	26 wks
ENROLMENT														
Pre-screening from research database	X													
Eligibility screen		X												
Informed consent		X												
Registration		X												
Physical Activity Readiness Quesionnaire (Par-Q) safety screening		X												
Allocation			X											
PHYSICAL INTERVENTION:														
Physical intervention visits				X	X	X		X		X		X		
Audio recording of physical intervention visit						X								
Physical Intervention Group: Review Health and Falls Record					X	X		X		X		X		
Physical Intervention Group: Review Exercise diaries							X		X		X			
Telephone calls (physical intervention)							X		X		X			
SOCIAL INTERVENTION:														
Social intervention visits				X	X	X		X		X		X		
Social Intervention Group: Review Health and Falls Record					X	X		X		X		X		
Telephone calls (social intervention)							X		X		X			
ASSESSMENTS:		X											X	X
Medication at baseline		X												

Social Support for Exercise		**X**												
UHDRS total motor scale, functional Assessment and Independence Scale		**X**												
Physical Performance Test		**X**											**X**	**X**
International Physical Activity Questionnaire (IPAQ)		**X**										**X**		**X**
LifeSpace Assessment		**X**										**X**		**X**
Lorig Self-Efficacy Scale		**X**											**X**	**X**
Self-reported Falls		**X**											**X**	**X**
UHDRS modified motor assessment		**X**											**X**	**X**
Six minute walk test		**X**											**X**	**X**
Timed Up and Go Test		**X**											**X**	**X**
EQ-5D		**X**											**X**	**X**
ICECAP-A		**X**											**X**	**X**
Symbol digit modality test		**X**											**X**	**X**
Verbal Category Fluency		**X**											**X**	**X**
PAS Healthcare climate questionnaire													**X**	

Table 2: Intervention Details described in line with the TIDIER framework for intervention description

1	NAME	Provide the name or a phrase that describes the intervention	***Engage-HD Physical Activity intervention***	***Engage-HD Social Interaction Intervention***
2	WHY	Describe any rationale, theory, or goal of the elements essential to the intervention	The ***Engage-HD Physical Activity intervention*** specifically focused on developing an individualized lifestyle approach to enhancing physical activity with interpersonal interactions of the physical activity coach underpinned by the concepts of self-determination theory (SDT). The function of the additional intervention components, namely a physical activity workbook and exercise DVD, were to facilitate education, enablement, modelling and goal setting.	The ***Engage-HD Social Interaction Intervention*** was a comparator intervention that provided conversational interaction. This social intervention was developed by our team in order to provide us with a comparator that could help us to both control for contact time and account for the potential influence of the interpersonal skills (i.e. relatedness) of the coach on any treatment effect while not focussing particularly on the goal setting processes inherent in a physical activity self-management intervention.
3	WHAT	Materials: Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers. Provide information on where the materials can be accessed (e.g. online appendix, URL).	This complex intervention consisted of 3 main elements, namely the *Participant/coach interaction (*underpinned by SDT), a purpose developed *ENGAGE-HD Workbook. The Workbook focused on disease specific information to facilitate exercise uptake, instructions on use of pedometers, and a goal setting section.* The exercise DVD (*Move to Exercise*) can be accessed online at: https://www.youtube.com/watch?v=6P-o4a6ht7Q&list=PLOi2wccX7y-YEC2Ww3IRiBbgAQ7YJmaSm; (accessed 18/01/2017).	Conversation cards (with images and text) representing a wide range of topics were used to help direct conversation toward topics of potential interest to the participants during each visit. In the first session, a 'getting to know you' conversation took place. Further discussions could focus on a range of topics including travel, media, food, music and art, entertainment, shopping, animals, science, technology, friends and socializing.
4		Procedures: Describe each of the procedures, activities, and/or processes used in the intervention, including	Participants enrolled in the ENGAGE-HD physical activity intervention received six home visits and interim telephone calls over a course of 14 weeks, during which time they were supported by trained activity coaches to develop an individualized, lifestyle approach to enhancing physical activity.	Participants enrolled in the ENGAGE-HD social interaction intervention received six home visits and interim telephone calls over a course of 14 weeks. At each face-to-face visit, the coach engaged with the participant in a talking and communication interaction

		any enabling or support activities.	During the first face-to-face visit, the coach introduced the participant to the ENGAGE-HD physical activity intervention, the workbook and the exercise diaries, which participants were asked to complete each week. The initial interactions considered benefits of physical activity and each participant's individual exercise history, as well as setting specific physical activity goals. Further discussion topics on physical activity included implementing a daily activity plan, monitoring exercise intensity, dealing with safety, weather, equipment and typical barriers (such as time, boredom, lack of equipment, lack of specific knowledge and support). In the remaining five home sessions, the coach continued to support discussions related to the activities in the workbook, and supervised the participant performing components of the Move to Exercise DVD exercise program or other physical activities. Coaches also reviewed exercise diaries completed during the previous week(s). Supportive telephone calls were conducted three times over the 14- week-period. These calls served to provide encouragement and advice with respect to the promotion of regular physical activity. During the calls, the coach also asked about any falls, health or medication changes and confirm the date and time of the next visit.	using purpose developed conversation cards (with images and text) representing a wide range of topics to help direct conversation toward topics of potential interest to the participants during each visit. Reminder telephone calls were conducted three times over the 14-week-period. These calls will served to match the contact time provided to the physical intervention group. During the calls, the coach asked about any falls, health or medication changes and confirmed the date and time of the next visit. At each home visit, the coach also completed a health and falls review with the participant where they will asked about (and recorded any details of) any falls, health professional interaction or medication changes.
5	WHO PROVIDED	For each category of intervention provider (e.g. psychologist, nursing assistant), describe their expertise, background and any specific training given.	Intervention delivery coaches were trained at a total of 8 sites. The coaches delivering the ENGAGE-HD physical activity interventions were either (a) health care professionals (e.g., Physical therapists (n=3), Occupational therapists, or Nurses (n=4)) with experience of delivering exercise-related activities or with specific experience with HD; or (b) exercise professionals (n=2). All staff had to meet specific health competencies, namely Skills for Life Competencies, developed by the National Health System (NHS) in the UK. (Competencies can be found at Skills for Life, accessed January 18, 2017: https://tools.skillsforhealth.org.uk/competence/show/html/id/2603/).	Intervention delivery coaches were trained at a total of 8 sites. The coaches delivering the ENGAGE-HD social interaction interventions were either (a) health care professionals (e.g. Occupational therapists (n=1), Nurses (n=7),) support workers with experience of delivering exercise-related activities (n=1), researchers with specific experience with HD (n=1); or (b) exercise professionals (n=2). The training model was for a team, including the intervention coordinator, trial chief investigator, and trial manager to travel to the site location and conduct a 6-hour training session in a small group setting. Coaches at sites received training in both interventions during this 6 hour session.

			The training model was for a team, including the intervention coordinator, trial chief investigator, and trial manager to travel to the site location and conduct a 6-hour training session in a small group setting. Coaches at sites received training in both interventions during this 6 hour session. Training for the physical coaches included a 1.5-hour, one-to-one session with either the chief investigator or the intervention coordinator. Both the chief investigator and the intervention coordinator were research physical therapists with extensive experience working with the HD community in both clinical practice and research, who oversaw development of the training materials and ongoing support of the coaching staff. A coach's manual was provided to each coach, and was used as a guide for each of the training sessions. The manual gave an explicit, session-by-session guide, familiarized the coaches with the specific challenges of working with patients with HD, and offered a background to the intervention's SDT framework. In addition to the initial training sessions and coaching manuals, coaches received ongoing support from the intervention coordinator. This support was particularly important in helping to guide coaches who have had little or no experience of working with patients with this relatively rare disease. Before each coach visited a participant for the first time, they were able to have a discussion with the intervention coordinator to assist them to interpret a participant's baseline assessment scores. This allowed them to appropriately anticipate the ability level and potential needs of each participant. After the initial home visits, coaches had a further discussion with the intervention coordinator to develop realistic goals for the participants, based on each participant's particular interests and their current ability levels. Coaches were further encouraged to contact the intervention coordinator if they had any questions about the home visits as the intervention progresses, either by e-mail or video-conferencing.	Training for the social coaches also included a 1.5-hour, one to-one training with the lead intervention coordinator prior to the start of the trial at each site, and the intervention coordinator was available for consultation throughout the trial. A coach's manual was provided to each coach, and was used as a guide for each of the training sessions. The coaching manual gave an explicit, session-by-session guide and familiarized the coaches with the specific challenges of working with patients with HD,

6	HOW	Describe the modes of delivery (e.g. face-to-face or by some other mechanism, such as internet or telephone) of the intervention and whether it was provided individually or in a group.	The physical activity sessions were delivered face-to-face. Supportive telephone calls were conducted three times over the 14- week-period.	The social interaction sessions were delivered face-to-face. Reminder telephone calls were conducted three times over the 14- week-period.
7	WHERE	Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features	The physical activity sessions were delivered in each participant's home.	The social interaction sessions were delivered in each participant's home.
8	WHEN AND HOW MUCH	Describe the number of times the intervention was delivered and over what period of time including the number of sessions, their schedule, and their duration, intensity or dose.	Participants received six home visits and 3 interim telephone calls over a course of 14 weeks. Mean face-to-face session duration was 58.3 (8.9) minutes. Mean duration of telephone calls was 10.1 (6.7) minutes.	Participants received six home visits and 3 interim telephone calls over a course of 14 weeks. Mean face-to-face session duration was 50.7 (2.7) minutes. Mean duration of telephone calls was 10.7 (6.7) minutes.
9	TAILORING	If the intervention was planned to be personalised, titrated or adapted, then describe what, why, when, and how.	The intervention was designed to be personalized to each individual by way of specific goal setting. Coaches worked together with participants to address individual barriers and facilitators to meeting goals. Goals were reviewed each session and the participant and coach worked collaboratively towards meeting the goals. Coaches also provided individualized advice regarding progression of exercise and physical activity.	There was no specific tailoring planned for the social interaction intervention.
10	MODIFICATIONS	If the intervention was modified during the course of the study, describe the changes (what, why, when, and how).	The intervention was not modified during the course of the study.	The intervention was not modified during the course of the study.

11	HOW WELL	Planned: If intervention adherence or fidelity was assessed, describe how and by whom, and if any strategies were used	Fidelity was measured by a combination of self-report checklists, independent assessment of the quality of the coaching sessions, based on audio recordings of the 3rd coach home visits. The fidelity of the coach interactions was measured by assessing the extent to which each coach demonstrated efforts to promote autonomy, relatedness, and competence, and a self-assessment completed by the intervention coaches. A set of 10 questions with a mix of rating scales (directly comparable to those scores used to rate fidelity) and free text answers were developed and delivered to the coaches via a web-based survey. The questions covered each coach's views on the training provided, adherence of the intervention to SDT, accompanying materials used in the delivery of the intervention, and the intervention in general. Respondents were asked to identify themselves so that their answers could be linked to individual fidelity scores.	Social intervention fidelity was assessed as total time spent in the home during the visit and length of interim telephone calls. This was chosen as the fidelity measure as we were looking to control for any confounds in relation to contact time. As a further evaluation, coaches were asked to record details of the conversations that we used to confirm the focus of discussions (and in particular to establish that the discussions were not related to physical activity).
12		Actual: If intervention adherence or fidelity was assessed, describe the extent to which the intervention was delivered as planned.	Mean (SD) interaction time spent in the home for the physical activity intervention across all visits was 58.3 (8.9) minutes. Mean (SD) time spent in discussion across telephone calls was 10.1 (6.7) minutes. Median (range) number of physical activity intervention visits completed were 6 (0-6). The self-report checklists completed by each of the coaches at the first home visit indicated that in 100% of sessions (16/16), coaches introduced the participants to the Physical Activity Workbook, gave the participants the exercise DVD and discussed the concept of goal-setting with the participant in 100% of the sessions. Sessions lasted on average 72.3 minutes. Fidelity scores for coach interactions, based on audio transcripts of the third intervention session, were assessed for 15 of the 16 participants. Overall scores ranged from 7 to 14 out of a possible 16 points, with a mean (standard deviation) score across the coaches of 11.0 (2.4). Coach interactions scored an average of 2.5/4 for autonomy, 3.0/4 for relatedness, 2.7/4 for competence, and 2.8/4 for the overall impression. Self-assessment scores were on average higher than those assigned by the independent rater, namely 3.1/4 for autonomy, 3.3/4 for relatedness, and 3.0/4 for competence.	Mean (SD) interaction time spent in the home for the social intervention across all visits was 50.7 (2.7) minutes. Mean (SD) time spent in discussion across telephone calls was 10.7 (6.7) minutes. Median (range) number of social activity intervention visits were 6 (3-6).

Table 3: Screening vs Recruitment by individual site

Site	Number of patients in Enroll-HD[1]	Number Screened (n)	Number Eligible (n)	% of screened considered eligible	Participants Recruited (n)			% of screened actually recruited	% of eligible actually recruited	Time to 1st recruited participant (days)	Time to last recruited participant (days)	Total time site open to recruitment (days)	Average length of time needed to recruit each participant (days)
					Total	Physical Activity	Social Comparator						
A	19	68	30	44	5	3	2	7	17	27	305	356	71.2
B‡	114	12	11	92	2	0	2	17	18	176	308	463	231.5
C‡*∞	52	19	4	21	4	2	2	21	100	49	301	309	77.3
D‡	269	9	6	67	6	3	3	67	100	61	392	392	65.3
E*∞	27	13	13	100	10	6	4	77	77	34	246	246	24.6
F∞	41	23	22	96	10	5	5	44	46	34	376	376	37.6
G∞	21	33	15	46	4	1	3	12	27	29	379	429	107.3
H*	146	72	14	19	5	2	3	7	36	66	251	336	67.2

1Registration as an Enroll-HD participant was a requirement unless the site could provide the medical history from clinical records. This number does not necessarily reflect the total number of HD patients serviced by the site but gives a good indication of the research active population at the site.
‡ Centres concurrently hosting major drug trials
* Centres with a physical therapist resident in clinic/ recruiting
∞ Site coordinator from within clinical team

Table 4: Baseline demographics and clinical characteristics split by treatment arm

Baseline demographics and clinical characteristics	**Physical Intervention** Mean (SD) or count (%)	**Social Control** Mean (SD) or count (%)	**Overall**
Age (years)	56.1 (10.3)	53.7 (9.9)	54.9 (10.1)
Gender (Male; Female)	12 (54.5%); 10 (45.5%) †	13 (54.2%); 11 (45.8%) †	25 (54.3%); 21 (45.7%) †
Height (m)	1.7 (0.1)	1.7 (0.1)	1.7(0.1)
Weight (kilograms)	77.3 (18.5)	73.8 (14.7)	75.5 (16.5)
Level of education			
CSE/GCE/GCSE school leaving certificate	9 (40.9) †	3 (12.5) †	12 (26.1) †
NVQ qualification	2 (9.1) †	5 (20.8) †	7 (15.2) †
A Level	1 (4.5) †	3 (12.5) †	4 (8.7) †
University degree	2 (9.1) †	4 (16.7) †	6 (13) †
Other	8 (36.4) †	9 (37.5†)	17 (37) †
Medication category			
Analgesic	3	6	

Antichoreic	12	8	
Antidepressant	19	19	
Antihypertensive	7	7	
Diabetes	0	3	
Other	25	25	
Functional score (maximum score=25)	16 (5)	18 (5)	17 (5)
Social Support – friends (maximum score=60)	15.0 (8.2)	17.0 (8.4)	16.1 (8.3)
Social Support – family (maximum score=60)	20.3 (8.5)	20.0 (9.1)	20.1 (8.7)

Table 5: Adjusted and unadjusted summaries of outcome measures at baseline, primary outcome assessment and follow-ups

		Baseline		Primary Outcome assessment		Difference at primary outcome *	Unadjusted 95% CI for the Difference.	Adjusted 95% CI for the Difference†
		Physical Intervention	Social	Physical Intervention	Social			
Physical Performance Test (PPT)		24.6 (6.5) (n=22)	24.9 (4.3) (n=24)	25.8 (5.6) (n=16)	25.0 (4.8) (n=22)	0.8	-2.8,4.3	-2.1 to 2.7
International Physical Activity Questionnaire (IPAQ)		1116.5 (1499.8) (n=21)	1299.8 (1626.9) (n=23)	2716.1 (2972.3) (n=15)	1357.8 (2262.9) (n=21)	1358.3	-521.2,3237.8	-22% to 653%#
Life Space		70.5 (25.7) (n=22)	60.8 (26.1) (n=24	79.5 (21.3) (n=15)	60.7 (25.1) (n=21)	18.7	2.9,34.6	-2 to 27
Self-efficacy (Lorig scale)	Exercise	6.4 (2.9) (n=22)	7.3 (2.5) (n=24)	7.6 (2.1) (n=17)	6.5 (2.7) (n=22)	1.1	-0.4,2.7	0.6 to 2.7
	Information	7.5 (3.2) (n=22)	8.1 (2.5) (n=24)	8.2 (2.2) (n=17)	8.1 (2.7) (n=22)	0.1	-1.4, 1.7	-1.3 to 1.6
	Help	7.4 (2.1) (n=22)	8.2 (1.6) (n=24)	8.0 (2.1) (n=17)	7.7 (1.7) (n=22)	0.3	-1.0, 1.5	-1.0 to 1.4
	Communication	8.4 (1.9) (n=22)	8.9 (1.4) (n=24)	8.8 (1.2) (n=17)	8.5 (1.7) (n=22)	0.2	-0.7,1.2	-0.4 to 1.2
	Manage disease	7.0 (2.5) (n=22)	7.2 (2.2) (n=24)	7.8 (1.7) (n=17)	7.0 (2.1) (n=22)	0.8	-0.5,2.0	-0.6 to 1.2
	Do chores	6.7 (2.7) (n=22)	6.5 (3.5) (n=24)	7.0 (2.6) (n=17)	7.1 (2.2) (n=22)	-0.1	-1.7, 1.5	-1.9 to 0.8
	Social	6.7 (3.1) (n=22)	7.1 (3.3) (n=23)	7.1 (2.8) (n=17)	7.0 (2.8) (n=22)	0.2	-1.6,2.0	-1.4 to 1.8
	Manage symptoms	6.5 (2.7) (n=21)	6.9 (2.5) (n=22)	7.3 (2.3) (n=16)	6.8 (2.6) (n=22)	0.5	-1.1,2.1	-1.0 to 1.6

	SOB	7.8 (2.3) (n=20)	8.2 (2.6) (n=20)	8.8 (1.6) (n=15)	7.7 (3.1) (n=19)	1.1	-0.6,2.8	-0.01 to 2.8
	Manage depression	6.9 (3.0) (n=22)	7.0 (2.6) (n=24)	7.6 (2.3) (n=17)	7.3 (2.3) (n=22)	0.3	-1.2,1.8	-1.2 to 0.6
UHDRS modified motor assessment		18.1 (7.4) (n=22)	17.2 (6.7) (n=24)	17.9 (6.4) (n=16)	17.6 (6.6) (n=23)	0.3	-4.0, 4.6	-2.1 to 3.4
6 minute walk (metres)		315.4 (132.9) (n=22)	344.2 (110.7) (n=24)	352.5 (103.2) (n=17)	334.8 (156.3) (n=23)	17.7	-65.5, 100.9	-20 to 109
Timed Up and Go Test (TUG) (seconds)		13.5 (8.9)(n=21)	11.1 (3.2) (n=24)	10.6 (2.0) (n=16)	11.2 (3.0) (n=23)	-0.5	-2.1,1.1	-2.6 to 0.3
EQ5D		0.7 (0.2) (n=22)	0.6 (0.3) (n=24)	0.7 (0.2) (n=17)	0.7 (0.3) (n=23)	0.1	-0.1,0.2	-0.12 to 0.11
ICECAP		0.8 (0.2) (n=22)	0.8 (0.2) (n=24)	0.9 (0.1) (n=17)	0.8 (0.1) (n=23)	0.0	-0.1,0.1	-0.06 to 0.03
Symbol digit modality test (correct)		18.3 (7.9) (n=22)	24.0 (8.9) (n=24)	21.6 (6.1) (n=17)	23.3 (10.7) (n=23)	-1.7	-7.1,3.8	0.01 to 5.9
Category Fluency		10.5 (3.7) (n=22)	12.4 (4.6) (n=24)	11.9 (4.4) (n=17)	12.0 (5.0) (n=23)	-0.1	-3.1,3.0	-1.3 to 2.7
PAS healthcare climate		-	-	6.0 (1.3) (n=17)	6.3 (1.1) (n=22)	-0.3	-1.1,0.4	-

* Physical – Social

†95% CI is adjusted for baseline Physical Performance Test (PPT), treatment arm, and all minimisation variables (age (less than 50/greater than or equal to 50), sex, Unified Huntington's Disease Rating Scale (UHDRS) total motor score (less than 45/greater than or equal to 45), site (Staffordshire, Birmingham, Manchester, Sheffield, Southampton, Aberdeen, Bristol, Cardiff))

The adjusted model log transformed the IPAQ so the adjusted estimates are presented as percentages

Figure 1: CONSORT Flow Chart