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## **A classification system to guide physical therapy management in Huntington's disease: a case series**

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## **Abstract**

Background and Purpose: Individuals with Huntington's disease (HD), a rare neurological disease, experience impairments in mobility and cognition throughout their disease course. The Medical Research Council Framework (MRC) provides a framework that can be applied to the development and evaluation of complex interventions, such as those provided by physical therapists. Treatment-based classifications, based on expert consensus and available literature are helpful in guiding physical therapy management across the stages of HD and contributing to the development and further evaluation of well-defined complex interventions in this highly variable and complex neurodegenerative disease. The purpose of this case series was to illustrate the use of these classifications in the management of two individuals with late-stage HD.

Case Description: Two females, ages 40 and 55, with late-stage HD participated in this study. Both experienced progressive declines in ambulatory function and balance as well as falls or fear of falling. Both individuals received daily care in the home for ADLs.

Intervention: Physical Therapy Treatment based classifications for HD guided the interventions and outcomes. Eight weeks of in-home balance training, strength training, task-specific practice of functional activities including transfers and walking tasks, and family/carer education was provided.

Outcomes: Both individuals demonstrated improvements that met or exceeded the established minimal detectable change (MDC) values for gait speed and Timed Up and Go performance. Both also demonstrated improvements on Berg Balance Scale and Physical Performance Test performance, with one of the two exceeding the established MDCs for both tests. Reductions in fall risk were evident in both cases.

Discussion: These cases provide proof-of-principle to support usage of Treatment Based

Classifications for physical therapy management for individuals with HD. Traditional classification of early-, mid-, and late-stage disease progression may not reflect patients' true capabilities; those with late-stage HD may be as responsive to interventions as those at an earlier disease stage.

Keywords: *Huntington's disease, gait, balance, falls, mobility; case series*

## Introduction

Huntington's disease (HD) is a progressive neurodegenerative disorder resulting in cognitive, motor and psychosocial dysfunction. Motor impairments lead to activity limitations related to walking, transferring and performing activities of daily living (ADLs). In addition to increased gait variability and slow walking,<sup>1</sup> individuals with HD experience deficits in anticipatory postural adjustments, postural responses, gait and static balance under changing sensory conditions<sup>2</sup> and while performing motor skills integral to ADLs.<sup>3</sup> As a result, these individuals are at increased risk for falls, and the sequelae resulting from subsequent mobility restrictions. More than 50% of individuals with HD are recurrent fallers, experiencing two or more falls per year.<sup>4,5</sup> Not surprisingly, recurrent HD fallers walk more slowly, perform more poorly on balance testing and are less physically active when compared to non-fallers with HD.<sup>4</sup> Motor impairments and increased fall risk contribute to loss of independence, social isolation, reduced self-esteem and loss of family role in individuals with HD.

Studies in HD animal models suggest that exercise improves motor function,<sup>6</sup> delays the progression of cognitive dysfunction,<sup>6</sup> and provides neuroprotection in the form of delayed disease onset.<sup>7,8</sup> In recent years, several small scale feasibility studies have investigated the effects of exercise and physical therapy in HD<sup>9-15</sup> with improvements observed in dynamic balance,<sup>9,10,11</sup> gait speed, function and level of physical activity,<sup>10,14</sup> fitness,<sup>13</sup> cognitive function,<sup>16</sup> neuroplasticity,<sup>16</sup> and self-reported quality of life measures.<sup>11,12</sup> These studies included early to mid-stage participants, and although they demonstrated proof-of-concept, were underpowered to establish efficacy. Full scale exercise trials are difficult to achieve in rare diseases, and are as yet outstanding for HD. To date, there are no reports of exercise interventions in mid to late-stage HD.

Response to exercise training and physical therapy in HD is variable; this may be due to a host of disease-related (i.e., disease variability, genetic predisposition, psychosocial) and environmental (i.e., carer support to gender, beliefs, socioeconomic status) factors. Another potential factor is the classification, or staging, system used to categorize patients is The United Huntington's Disease Rating Scale (UHDRS) Total Motor Score (TMS)<sup>17</sup>. UHDRS-TMS is a subjective evaluation of motor impairments, encompassing bradykinesia, chorea, dystonia, motor impersistence, balance and gait. The Total Functional Capacity (TFC) Scale is a more global scale of functional status, encompassing occupation, finances, domestic chores, ADLs and care level. Scores on the TFC range from 0-13, and patients are typically categorized as early stage (10-13), mid stage (7-9), and late stage (0-6). Because of the range of items and scoring criteria, individuals with the similar overall UHDRS-TMS or TFC scores can present quite differently. Furthermore, the TFC is not related specifically to movement and is limited to a categorical assessment of levels of assistance. Thus, a stratification system to better understand clinical subtypes and guide physical therapy intervention is needed.

An enduring question in physical therapy (PT) practice is whether, and to what extent, the interventions that form part of standard practice are effective and efficient. Lack of clear definitions and categorization of intervention components, as well as inconsistency in the terminology applied in published trials, limits not only our understanding of the active ingredients of interventions but also the replication thereof. Furthermore, knowledge translation is difficult and this limits opportunities for research to inform clinical practice and vice versa. The Medical Research Council (MRC) of the United Kingdom provides a framework for developing and evaluating complex interventions<sup>18,19</sup> as well as incorporating process evaluations to better understand context-driven mediators of outcome<sup>20</sup>. Intervention

development begins with identifying evidence, theoretical component, and modeling process and outcomes (see Figure 1). Where appropriate, this should extend from pre-clinical studies to qualitative inquiry that iteratively inform subsequent feasibility and acceptability studies. Efficacy and implementation only occurs after a comprehensive process of development and feasibility testing.

<Figure 1 here>

In totality, the guidance calls for transparent development of theoretically driven interventions, the use of qualitative methods to support intervention development and evaluation, and monitoring of intervention delivery. Importantly, there should be flexibility in the stages of development such that piloting, evaluation and implementation develops based on emerging evidence.

In an effort to facilitate the development of theoretically driven interventions in HD, our group has developed Physical Therapy Guidelines for HD that utilize Treatment Based Classifications (TBCs)<sup>21,22</sup> (Table 1). These TBCs define the primary activity deficits and underlying impairments of individuals with HD, group individuals by their response to interventions, and provide recommended interventions and outcome measures to monitor longitudinal change. In theory, TBCs<sup>23,24</sup> provide a useful scale to guide treatment decisions and determine rehabilitation goals following physical therapy evaluation of specific symptoms and activity deficits and determination of the classification that best fits their client's individual needs. The TBCs were developed by expert consensus and guided by available literature, with the purpose of guiding clinical decision-making. An important goal of the TBCs was to further validate the classifications utilizing case studies and clinical trials. Therefore, the objective of this case series is to describe the physical therapy intervention and outcomes for two individuals

with late-stage HD, and to apply their intervention to the TBCs developed for HD. With a paucity of exercise interventions including individuals with late-stage HD, single case studies may provide useful information and proof-of-principle of the beneficial components of physical therapy interventions.

<Table 1 here>

## **Case Description**

### *Participants*

Both participants were in the late-stage of HD, as defined by TFC scores (Table 2) and receiving regular clinical care at the Cardiff Huntington's disease Research and Management Clinic. Participants were consented under parent studies; Case 1 was assigned to the control arm of the TRAIN-HD study (Ethics: NHS REC 12/WA/0151).<sup>12</sup> The control arm received a modified version of the intervention after completion of the study, but was excluded from the analysis as she was unable to complete the minimum dataset. For those in the control group, participants were seen 1-2x/week, and received a modified version of the protocol, which allowed for more independent decision-making by the therapist. Case 2 was assigned to the intervention group of Move to Exercise (Ethics: 09/WSE02/24) and received the intervention as defined by the study protocol.<sup>10</sup>

### Case 1 (AA)

#### *History*

AA was a 40-year-old female diagnosed with HD at age 34. At evaluation, she was housebound, required assistance with all functional activities, did not work, and lived with her

husband and 6-year-old daughter in a two-story home. She had a carer available for 15 hours daily. AA's medical history was unremarkable. Her medications are listed in Table 2.

Over the past several years, AA experienced a progression of symptoms, and was referred to physical therapy to address her primary activity limitations of poor balance, difficulty with ambulation, and transfers complicated by reduced aerobic capacity and poor motivation.

<Table 2 here>

### *Exam*

At evaluation, AA presented with moderate to severe rigidity throughout her trunk, upper and lower extremities. AA was able to maintain unsupported static standing balance for a short period but required assistance of one person during additional movements or with perturbations. Her strength was 4/5 throughout and gait was notable for a wide base of support, dystonia in bilateral feet (inversion and mild plantarflexion), bradykinesia, and akinesia with initiation of movement slow and effortful. AA was able to ambulate with assistance of one person over three meters but used a wheelchair for community mobility.

AA's carers performed all personal and domestic ADLs. AA was unable to roll or move from lying to sitting or sitting to lying. She required moderate assistance to rise from a chair. Prior to this evaluation, she had been labeled a "high handling risk" by the Manual Handling Risk Assessment required by the UK Health and Safety at Work Act Regulations (1974). As a result, electronic adaptations and aids were utilized by her carers, and her mobility was limited to short indoor distances with assistance. The therapist also noted apathy and lack of engagement in daily activities. Mobility was assessed as described in the Outcomes section below and in Figures 2 and 3.

## Case 2 (BB)

### *History*

BB was a 55-year-old female diagnosed with HD at age 50. At evaluation, she required assistance to manage her finances, home maintenance, and food preparation. BB did not work, lived alone in a first-floor apartment, and had a carer 4 days per week to assist with ADL activities. Her past medical history is notable for depression, hyperthyroidism and hypertension. Her medications are listed in Table 2.

Over the past five years, BB experienced a gradual progression of symptoms, and was referred to physical therapy by her neurologist. Her primary activity limitations were poor balance and difficulty walking independently. BB's primary concern was fear of falling following a previous fall that resulted in multiple injuries and hospitalization.

### *Exam*

BB was independent with dressing and bathing, but used a walker for ambulation inside the home and a wheelchair for community mobility. Her mobility was assessed as described in the Outcomes section below and in Figures 2 and 3.

## Outcome Measures

### Measures of Activities

**Physical Performance Test.** The Physical Performance Test (PPT)<sup>25</sup> requires individuals to perform nine tasks that mimic basic to standard activities of daily living. Each item is rated on a 4-point scale for a maximum score of 36. The PPT is an appropriate measure of function in individuals with HD<sup>26</sup> that demonstrates excellent test-retest reliability in individuals with manifest (i.e., motor symptoms are present) HD and has an MDC of 5.<sup>27</sup>

**Walking Speed.** During the 10-meter walk test (10MWT),<sup>28</sup> participants ambulate at their self-selected comfortable pace across 14 meters; 2 meters to allow for acceleration, 10 meters where their time to walk is measured, and 2 meters to allow for deceleration. The time to complete the 10 meters is recorded and gait speed (distance/time) is calculated. The 10MWT gait speed measure has excellent test-retest reliability and an established MDC of 0.3 m/s for individuals with HD.<sup>27</sup>

**Timed Up and Go.** The Timed Up and Go (TUG)<sup>29</sup> requires participants to stand from a chair, walk 3 meters, turn, and return to a seated position in the chair. The participant performs one practice and one test trial, and the time to complete the task is recorded. The TUG is a good disease-specific measure of mobility in HD<sup>26</sup> with excellent test-retest reliability and an established MDC of 2.98 seconds in individuals with HD.<sup>27</sup> Individuals with HD are at increased risk of falls if TUG  $\geq$ 14 seconds.<sup>4</sup>

**Six-Minute Walk Test.** The 6-minute walk test (6MWT)<sup>30</sup> was collected in Case 1 only as a measure of walking endurance. During the 6MWT, an individual ambulates for 6 minutes and the total distance in meters is recorded. The 6MWT has good-excellent test-retest reliability and an established MDC of 86.57 meters in individuals with HD.<sup>27</sup>

#### Measures of Impairments in Body Function

**Berg Balance Scale.** The Berg Balance Scale (BBS)<sup>31</sup> is a 14-item scale that assesses static balance performance. Quality of performance on each item is scored using a 4-point scale, for a maximum score of 56. The BBS is a good disease-specific mobility measure in HD<sup>26</sup> that has excellent test-retest reliability in individuals with HD and MDC of 5 for individuals with manifest HD.<sup>27</sup> Individuals with HD are at increased risk of falls if BBS  $\leq$ 40.<sup>4</sup>

**Four Square Step Test.** The Four Square Step Test (FSST)<sup>32</sup> was collected in Case 2 only as a measure of dynamic standing balance. The FSST requires an individual to step over four canes, placed in a cross configuration on the floor, in a specific sequence (forward, right, backward, left), and then repeat this sequence in the reverse order. The time to complete this task is recorded as the final score. The FSST has good test-retest reliability and an established MDC of 15.27 seconds in individuals with manifest HD.<sup>27</sup>

### Measures of Quality of Life

**Short Form-36.** The Short Form-36 (SF-36)<sup>33</sup> was collected in Case 2 only to assess health-related quality of life in both the mental and physical domains. The SF-36 is reliable and valid for individuals with HD and their carers.<sup>34</sup>

## **Intervention**

Despite enrollment in parent studies, both cases met criteria for classification in TBC C: Mobility, Balance and Falls Risk, in the HD Clinical Guidelines, including interventions such as balance training, strength training, task-specific practice of functional activities including transfers and walking tasks, and family/carer education (see Table 1, and also Table C from <http://www.futuremedicine.com/doi/pdf/10.2217/nmt.11.86>).<sup>22</sup>

### *Case 1.*

AA received one-on-one physical therapy for 8 weeks, delivered 1x/week for 1 hour. The program consisted of home-based physical therapy focusing on walking, balance and transfer practice. The therapist also educated and trained the family and carers. The intervention focused on three main concepts: a) mobility and skills training; b) motivation and goal-setting; and c)

opportunity and enablement. Between physical therapy visits, the lead carer conducted independent sessions for 1 hour/day over the 8-week intervention.

Mobility training consisted of task-specific balance and strength training in functional transfers, gait, reaching, bed mobility, stair-climbing and turning. To progress the difficulty, gait was performed both indoors and outdoors, car transfers were practiced, turning was performed in tight spaces, and the time spent on each activity was increased to build endurance. An emphasis was placed on simple verbal instructions and positive reinforcement.

The motivation component of the intervention consisted of setting achievable, meaningful goals to allow AA to demonstrate her abilities and build confidence. An ultimate goal of a family holiday motivated AA to participate in functional tasks and outdoor ambulation.

The opportunity component of the intervention focused on enabling AA to participate in her daily life, family life, and physical activities.

#### *Case 2.*

The intervention for BB took place within BB's home also over a period of 8 weeks, and was focused on the following concepts: a) gait and postural control; b) functional mobility; c) health-related quality of life. BB was instructed to perform exercises at home 3x/week using a purpose-developed exercise DVD<sup>35</sup> (please see [https://www.youtube.com/channel/UCH7\\_ed2\\_\\_mkzXNWPZqVIosw](https://www.youtube.com/channel/UCH7_ed2__mkzXNWPZqVIosw) for videos). Briefly, the DVD consisted of 5 sections: a) warm-up and flexibility; b-d) strength and balance exercises tailored specifically for individuals with HD; e) cool down and relaxation. The balance exercises were divided into two sections. The first section focused on practicing narrowed and altered functional base of support exercises. The easiest of the exercises required the participant to maintain balance while the heels and toes of the feet were touching. To progress the difficulty,

these movements were performed with eyes closed, standing on one leg, tandem stance, or during forward and side lunges. Level of support was also progressed from holding onto a table/chair to using support only as needed. The second section of balance exercise focused on performance of task-specific activities that required alterations of dynamic balance, such as transfers from sitting to standing, turning, and stepping up onto stairs. To progress the difficulty, the number of repetitions was increased and the number of rest breaks was decreased.

During an initial home visit, the therapist taught each exercise to the participant and instructed BB on how to progress the exercises. The therapist also discussed the benefits and precautions for each exercise. All instruction took place in the presence of a carer, who agreed to assist BB as needed. In addition to performing the DVD exercises, BB also began a 30-minute gradual progressive walking program, by walking 1x/week on level ground around her home and neighborhood. She was instructed to walk at her self-selected comfortable pace and to take rest breaks as needed. She was encouraged to progress her walk by increasing the time walked until she reached 30 minutes. BB was asked to keep a record of her daily exercise program in an exercise diary.

The therapist called BB weekly to monitor her progress and discuss any issues.

## **Outcomes**

### *Case 1- AA.*

AA demonstrated marked improvements in function following 8 weeks of physical therapy intervention. AA's performance on the PPT improved from 4 to 16; her BBS performance improved from 22 to 45 and her TUG performance improved from 47.2s to 33.3s following training. Similarly, gait speed and endurance also improved; at baseline AA was not

walking, but following training, she ambulated at 1.18m/s and walked 297.4 meters during the 6MWT (Figures 2-3).

AA's carer was actively involved in the intervention, advocating on her behalf and encouraging AA to engage in training on days when the physical therapist was not present. Qualitatively, AA's carer noted that although she still required close supervision and occasional assistance:

*“She does the weekly shopping herself, she goes out, she collects her prescriptions, everything that she needs that now has made her become a wife and mother...again. Since she's been doing exercises, speech has improved as well.”*

#### Case 2-BB.

BB also demonstrated improvements in function following 8 weeks of physical therapy intervention. BB's performance on the PPT improved from 13 to 15; her BBS performance improved from 45 to 47, and her TUG performance improved from 22.8s to 13.9s following training. She also demonstrated marked improvements in gait speed, ambulating at 0.39m/s prior to training and 0.72 m/s post-training. Additionally, she completed the FSST more quickly following training (12.6s pre; 11.9s post) and reported improvements on the physical functioning subscale of the SF-36 with a rise from 20 to 75 (Figures 2-3).

BB's carer was actively involved in supporting the walking program, where her adherence was excellent, and went above the suggested amount of 30 minutes per week, walking 3 times per week for 30-40 minutes total as part of shopping trips with her carer. Conversely, BB did not experience as much support from her carer in completing the exercises shown in the DVD, and her adherence rate with the exercise DVD was 2/24 (8.3%). Qualitatively, BB's carer reported:

*“There is a big improvement from the first time I saw her [two months ago], she is no longer using the wheelchair. She walked from the car park to [the laboratory] today and I would say that is a big improvement.”*

<Figures 2 & 3 here>

### **Discussion**

The purpose of this case series was to demonstrate the use of TBCs to guide physical therapy treatment planning for two individuals with HD. Both individuals presented with primary activity limitations in mobility, balance, and falls risk (TBC C; Table 1) and demonstrated improvements in function following 8-weeks of physical therapy targeting gait, balance and fall risk reduction. Both AA and BB met the MDC values established for late-stage HD for gait speed and TUG, with increases in gait speed of 1.18m/s and 0.33 m/s, respectively and reductions in time to complete the TUG of 13.9 seconds and 8.9 seconds, respectively (Figure 2A-B). While BB demonstrated improvements on the BBS and PPT, only AA exceeded the established MDCs for late-stage HD with improvements of 23 points and 12 points, respectively (Figure 2C-D). Furthermore, both AA and BB experienced changes in function that indicate a reduced fall risk. BBS scores  $\leq 40$  indicate increased fall risk for individuals with HD;<sup>4</sup> following training, AA moved from a BBS score of 22 to 45, marking a change in fall status from high risk to lower risk. Similarly, individuals with a TUG score of  $\geq 14$  seconds are at higher risk for falls;<sup>4</sup> following training, BB moved from a TUG of 22.8s to 13.9s, demonstrating a shift to lower fall risk. These improvements are particularly notable given that both individuals were the later stage of HD.

Within the guidelines of TBC C, the general aims of physical therapy are to: a) improve mobility status by increasing independence, gait speed and distance walked; b) reduce risk of

falls or actual falls; c) maintain independent transfers and walking; and d) reduce fear of falling.<sup>17</sup> Although AA and BB both demonstrated improvements in gait, balance and function following 8 weeks of task-specific training, one notable difference in these cases was the involvement of the primary carer. While AA's carer was involved in all aspects of the intervention, BB's carer actively supported only the walking program. Their adherence results support prior work stating that individuals with HD experience more success with exercise when their caregiver is actively involved in the intervention<sup>35</sup> and highlight the importance of carer support and encouragement for task-specific practice (i.e., walking).

At initial development, we anticipated that the TBCs would have a relationship with disease stage. The TBCs had sub-categories related to premanifest (TFC 13; no clinical signs of HD), early (TFC 10-13), middle (TFC 7-9) and late stages (TFC 0-6). Thus, our original paper introducing the TBCs suggested that TBC C was applicable to individuals in early-mid stage HD.<sup>22</sup> However, as this case series shows, individuals with late-stage disease can still be functional and respond to similar interventions as those in earlier disease stages. This case series extends the literature to demonstrate that later-stage clients with HD may benefit from physical therapy services under TBC C and should be referred to physical therapy when (or before) they experience declines. These cases provide proof-of-principle to support the use of TBCs to guide physical therapy management for individuals with HD. Although the TBCs require further validation across disease stages, the clear guidelines within each classification have the potential to address two key barriers identified by therapists treating individuals with HD: insufficient use of routine physical therapy-related outcome measures at different stages of HD<sup>36</sup> and clearer reporting of intervention protocols so as to generate a better understanding of the impact of exercise and physical therapies on the symptoms of HD.<sup>37</sup> Given the changing nature of HD and

the variability associated with functional deficits, TBCs have the potential to inform treatment planning, intervention development and subsequent evaluation in line with the MRC framework for complex interventions.

### *Limitations*

Despite the favorable outcomes reported, the case series design limits us from drawing conclusions about the benefit of physical therapy for all individuals with late-stage HD. We acknowledge that some of the benefits may be from social contact with the physical therapists, but this effect was not directly measured. Prospective recordings of falls following the interventions were not obtained, so it is unknown if these task-specific interventions influenced future fall risk. TBC C recommends interdisciplinary consultations, including occupational therapy, nutrition, and speech therapy, which were not utilized in these studies and may have further improved more global outcomes in these participants. Additionally, these cases demonstrate the implementation of outcomes and interventions with regard to only one of the TBCs; future work should not only validate the TBCs, but examine their utility across disability levels and with regard to current evidence-based literature.

### **Summary**

This study provides proof-of-principle that physical therapy for mobility, balance, and fall risk is feasible and confers benefit for some individuals with late-stage HD. Larger studies with a control group are necessary to confirm these outcomes, and future work should examine the validity of the TBCs to inform physical therapy management of individuals with HD.

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**Table 1. Treatment Based Classifications**<sup>21,22</sup>

<b>Classification</b>	<b>Description</b>
A. Exercise capacity and performance	Absence of motor impairment or specific limitations in functional activities; potential for cognitive and/or behavioral issues
B. Planning and sequencing of tasks (including bradykinesia)	Presence of apraxia or impaired motor planning; slowness of movement and/or altered force generation capacity resulting in difficulty and slowness in performing functional activities
C. Mobility, balance and falls risk	Ambulatory for community and/or household distances; impairments in balance, strength, or fatigue resulting in mobility limitations and increased falls risk
D. Secondary adaptive changes and deconditioning	Musculoskeletal and/or respiratory changes resulting in physical deconditioning, and subsequent decreased participation in daily living activities, or social/work environments
E. Abnormal posturing (seating and bed positioning)	Altered alignment due to adaptive changes, involuntary movement, muscle weakness and incoordination resulting in limitations in functional activities in sitting
F. Respiratory dysfunction	Impaired respiratory function and capacity; limited endurance, impaired airway clearance resulting in restrictions in functional activities and risk for infection

G. Palliative Care

Active and passive range of motion limitations and poor active movement control resulting in inability to ambulate; dependent for most activities of daily living; difficulty maintaining upright sitting position

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**Table 2. Case Characteristics at Baseline**

	<b>Case 1-AA</b>	<b>Case 2-BB</b>
<b>Age (yrs)</b>	40	55
<b>Gender</b>	Female	Female
<b>Symptom Duration (yrs)</b>	6	5
<b>UHDRS-TMS</b>	74	Not assessed
<b>TFC</b>	2	5
	Vesicare (overactive bladder)	Carbimazole (hyperthyroid)
	Lansoprazole (heartburn)	Paroxetine (depression)
<b>Medications (indication)</b>	Clonazepam (involuntary movements)	Ramapril (hypertension)
	Sertraline (depression)	Propranolol (hypertension)

Full UHDRS-TMS was not assessed for Case 2. Total Functional Capacity (TFC); Total Motor Score (TMS); United Huntington’s Disease Rating Scale (UHDRS).

Figure 1: Medical Research Council (MRC) framework for Developing and Evaluating Complex interventions (Adapted by permission from BMJ Publishing Group Limited, license number 3912151415579).

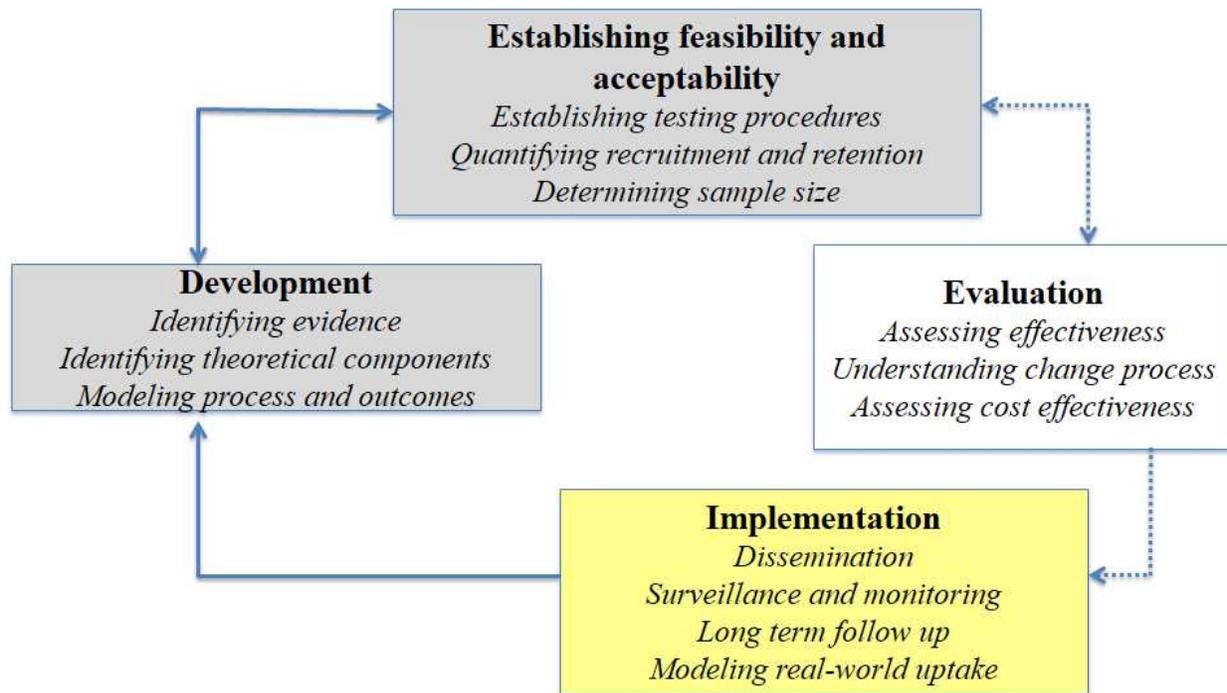


Figure 2. Both individuals with late-stage HD experienced improvements in A. gait speed; B. Timed Up and Go performance; C. Berg Balance Scale performance; and D. Physical Performance Test scores. Both cases experienced improvements that surpassed the established MDC for late-stage HD for gait speed and Timed Up and Go, while Case 1 also had improvements on the Berg Balance Scale and Physical Performance Test that surpassed the MDC. \* Indicates that improvements in performance met or exceeded established MDC values for late-stage HD.

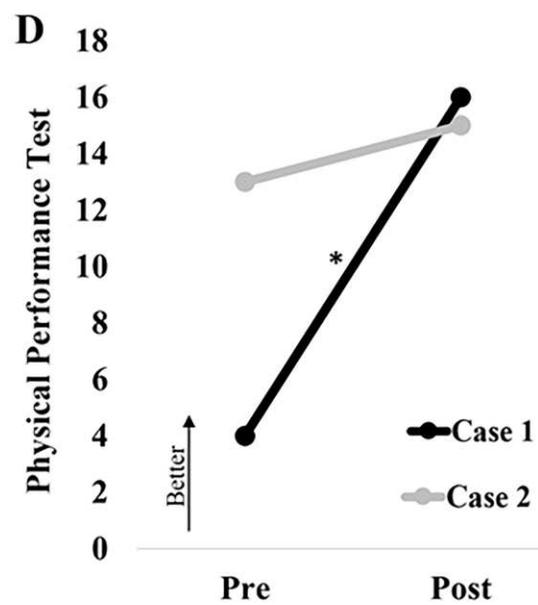
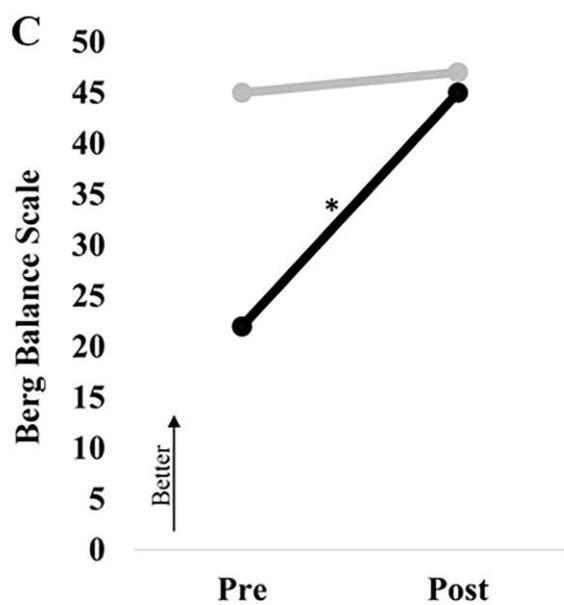
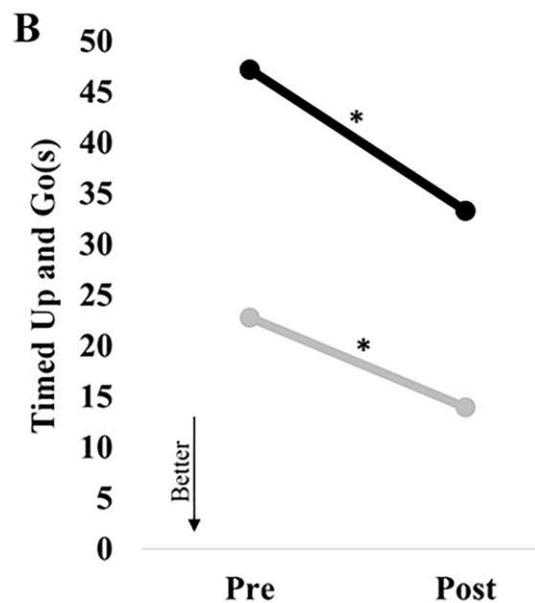
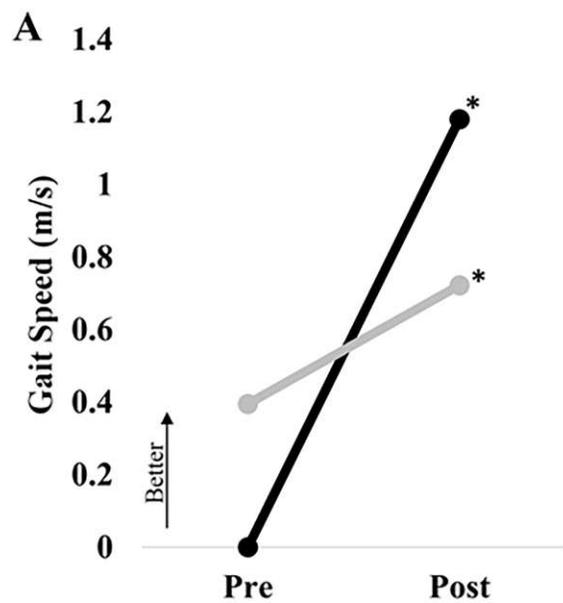


Figure 3. A. The individual in Case 1 experienced a marked improvement on the 6-minute walk test that far exceeded the established MDC for late-stage HD, while the individual in Case 2 experienced improvements in B. Four Square Step Test performance, and C. physical quality of life as measured by the SF-36 Physical Function Subscale. \* Indicates that improvements in performance met or exceeded established MDC values for late-stage HD.

