Research Article   **Open Access**

Effects of an Inpatient Multidisciplinary Intervention on Physical Ability and Self Perceived Health Status in Multiple Sclerosis and Parkinson's Disease Patients

Bjornar Berli, Randi Dalen, Bente Oldren, Torbjorn Rundmo[*]

Department of Psychology, Norwegian University of Science and Technology Trondheim, Norway

[*]**Corresponding author:** Torbjorn Rundmo, Department of Psychology, Norwegian University of Science and Technology Trondheim, Norway, Tel: +47 90652152; E-mail: torbjorn.rundmo@ntnu.no

Abstract

Objective: The current study's objectives were to investigate the effects of a multidisciplinary intervention (MDI) for multiple sclerosis (MS) and Parkinson's disease (PD) patients on physical ability and self-perceived health status, and to examine the relationship between physical ability and health status in these patient groups.

Methods: 110 patients (44 with PD, 66 with MS) were enrolled in a 4-week inpatient MDI program. Measures of health status (SF-12) and physical ability (6 min walking, timed up-and-go test, and sit-to-stand test) were administered before and after intervention.

Results: The results showed significant improvements on physical performance and increased physical and mental health status in both patient groups. Physical health status (PCS) correlated significantly with all three physical tests. Physical test scores showed a significant predictive value on PCS. Few previous studies have explored the effects of short, intensive, inpatient treatment programs on quality of life measures in these patient groups. Results of the current study suggest that the short intensive inpatient rehabilitation is effective in producing short term improvements.

Conclusion: The conclusion is multiple sclerosis and Parkinson's disease patients seem to benefit from a multidisciplinary intervention, improving both objective and subjective perceptions of health. As expected, physical ability was closely related to perceived physical health, but not mental health, highlighting the importance of addressing psychological symptoms separately in treatment. Knowing the heterogeneity of among the two groups of patients regarding symptoms and disability, finding an 'ideal' intervention across patients is nearly impossible. This variation within the patient groups makes studying mechanisms of change, or pathways leading to improvements in quality of life, difficult. Two plausible mechanisms are proposed: First, improvements on the level of physical function may influence health status positively. Secondly, the holistic, multidisciplinary approach to treatment may target non-motor factors important to patient-perceived health status. The results of the current study also supported a holistic multidisciplinary approach to treatments for Parkinson's disease and multiple sclerosis patients.

Keywords: Multiple sclerosis; Parkinson's disease; Physical performance; Physical ability; Self-perceived health status; Multidisciplinary approach; Quality of life; Programme evaluation

Introduction

Multiple sclerosis (MS) and Parkinson's disease (PD) are two common chronic progressive neurodegenerative diseases. MS is characterized by a loss of myelin in the central nervous system due to a chronic inflammatory autoimmune response. Demyelination and axonal loss disrupts communication within the nervous system resulting in a wide array of symptoms which may include various cognitive and affective impairments, tremors, clumsiness and poor balance, stiffness, bladder dysfunction, impotence, constipation, impaired vision, speech impairments, pain and fatigue [1]. Parkinson's disease is characterized by a loss of dopamine-generating cells in the substantia nigra, although the mechanisms behind this degeneration are unknown. Cardinal symptoms of PD include bradykinesia, or slowness of movement [2], weakness, tremor, rigidity and postural instability [3]. Although motor symptoms are the most recognizable symptoms of PD, especially in its early stages, various cognitive and emotional problems are also common. These include depression, constipation, pain, sleep disorders, genitourinary problems, sensory difficulties, and in later stages dementia [4].

The demographics of the two diseases differ. MS affects women more than men and has a relatively young age of onset. PD affects men more than women and generally has a much older age of onset. With advances in treatment, people with MS are living longer and most PD patients will have a survival close to normal [5]. However, patients do become increasingly impaired as the degeneration progresses.

The nature of MS and PD make the people affected susceptible to a lower 'quality of life' (QOL) than the normal population. Benito-Leon et al. [6] identified several factors of MS which are especially taxing on patients' psychological and social well-being, including early onset of the disease, unstable properties of the condition, effects on higher cognitive functions, the relative preservation of insight and the absence of good treatments. In people with PD, motor symptoms such as falls,

restrictions in mobility and dyskinesia, as well as emotional disturbances, social embarrassment, and sleep disturbances have been indicators of reductions in QOL [7]. QOL measures should be an essential part of assessing symptoms and treatment for MS and PD patients.

There is no consensus on a single definition of quality of life. Health research commonly distinguishes between the patient-based outcomes of quality of life (QOL), health-related quality of life (HRQOL), and self-perceived health status (HS). The broad construct of QOL is defined as a subjective global judgement of satisfaction with life [8,9], differentiating it from umbrella-terms containing multiple facets. The advantage of a simple, singular definition is in the possibility of elevating the QOL concept to a psychological construct to drive theory [9]. The disadvantage of a global definition is not capturing nuances of people's experiences in different areas of their lives, becoming too general a concept for clinical populations [10]. This is captured by other definitions of QOL as an umbrella-term containing a variety of important concepts, including physical health, psychological state, social functioning, health status, levels of independence, life conditions, spirituality etc. [11]. The main issue with such an umbrella term is in the heterogeneity of domains contained under the umbrella. As a multifaceted term, QOL has no consistent definition (i.e. different instruments include different domains), but comes closer to capturing the important experiences of patients [9]. Rejeski and Mihalko [9] label the umbrella-term of QOL as HRQOL. Others define HRQOL as a narrowing of the QOL concept to those aspects of life quality which are influenced by health status or by the impact of illness [7,12].

Adverse symptoms as well as management and treatment of chronic diseases lead to a variety of difficulties for patients, across physical, mental, social and behavioral plains. HRQOL examines how these difficulties affect the individual's life in ways that are important to the individual [13]. However, when a patient is ill, almost all aspects of life can become health related [14]. The distinction between general QOL and HRQOL can therefore become artificial, especially in patients with chronic diseases such as MS and PD, as it becomes impossible distinguish between parts of their lives influenced by their health condition and parts that are not [15].

QOL as well as HRQOL focus on subjective limitations and experiences, but also include valuations of the impact of those limitations and experiences on the subject's life [13]. This second valuation is not included in the HS-construct, which is a more descriptive measure of physical and mental symptoms and limitations [16]. HS measures subjective appraisals of a person's ability to perform various physical, emotional and social activities [17]. It can measure function on either a generic or disease-specific level, depending on the questionnaire used. HS is a subjective measure of health. It should be considered a determinant of QOL/HRQOL, but should not be used directly as an indicator of QOL itself [16,18] as it lacks judgements about the impact of well-being and individual expectations [19].

A major challenge and point of criticism in the field of quality-of-life research is the ambiguity of the terms and lack of uniformity in tools [16,8,20]. There are examples where QOL and HS are used interchangeably [21]. Also, the same questionnaire (e.g. SF-12) is sometimes labeled as measuring HRQOL [22], and other times labelled as a HS-measure [13,23], attesting to the ambiguousness of the tools used to measure QOL constructs. This makes the interpretation of results across a broad range of studies difficult. This paper focuses on the quality of life construct most closely related to objective function; self-perceived health status. However, research on HRQOL using similar questionnaires to HS, as well as systematic reviews encompassing both constructs are still highly relevant to the current research questions.

Although MS and PD are chronic and progressive diseases with impact on QOL and widespread motor symptoms, there is broad support for the effect of exercise in improving the physical abilities of these patient groups. Systematic reviews on physical exercise for people with MS have concluded that there is high quality evidence for exercise and physical activities improving motor-function outcomes, including mobility, muscle strength and aerobic capacity [24-26]. A meta-analysis of exercise in MS patients found exercise interventions to be associated with a 10% increase in muscular fitness outcomes, and 18% increase in cardiovascular outcomes, and effect was deemed clinically meaningful [27]. Similar positive effects of exercise interventions on physical functioning have also been found in people with PD [28,29].

If exercise can limit physical deterioration, or even improve motor functions in people with MS/PD, quality of life may also be affected. Several previous studies have investigated changes in HS and HRQOL in people with MS. Latimer-Cheung et al. [25] reviewed 21 previous studies on the effects of exercise on HS/HRQOL in MS patients. Although the constructs are similar, it is important to distinguish between them, especially between HS and QOL/HRQOL. A meta-analysis by Smith et al. [30] concluded that HRQOL and HS are two distinct constructs which should not be used interchangeably. Other research has indicated HS to be a mediator between physical activity and QOL [23].

The effect of exercise on HS/HRQOL has also been investigated in people with PD. In a systematic review, Goodwin et al. [28] identified four previous randomized controlled trials on the effects of exercise on HRQOL/HS [31-34], using a variety of HRQOL outcome measures. Of these, only one study [34] reported a significant increase in HRQL (measured by EQ-5D) due to exercise intervention. However, Goodwin et al. [28] synthesized the relevant data from all 4 studies, with a total of 292 participants, and found a standardized mean difference of 0.27, 95% CI 0.04–0.51, suggesting that exercise interventions are likely to result in improvements on HRQOL/HS. Although people with MS/PD have been found to both tolerate and benefit physically from exercise, it seems the effect on HS/HRQOL is limited and poorly supported.

Even though the effect of physical exercise on HS/HRQOL is limited, the relationship between disability/physical ability and HS/HRQOL is widely supported. HS/HRQOL has been shown to decrease as disability in MS patient's increases. Henriksson et al. [35] split a population of MS patients into three groups based on disability (measured by EDSS: Kurtzke Expanded Disability Status Scale), and found a significant difference in HS/HRQOL (measured by EQ-5D) between the groups. Benito-Leon et al. [36] found significant correlations between EDSS scores and all 6 dimensions of FAMS HRQOL (Functional Assessment of Multiple Sclerosis), and Pfennings et al. [37] found that severity of MS (EDSS score), time since diagnosis, and recent MS progression had an effect on HRQOL. In PD patients, a wide array of functional ability measurements (including Timed Up-and Go test [TUG], 6 min walking, Freezing of Gait Questionnaire [FOG-Q], and Movement Disorder Society Revision of the Unified Parkinson's Disease Rating Scale [MDS-UPDRS]), as well as disease severity (Hoehn and Yahr stage) have been found to both correlate with, and significantly predict changes in HS/HRQOL [38-42]. The strongest relationships were found between physical ability and the mobility-related subgroups of HS/HRQOL measures, i.e. PDQ-M and SF-36 PCS [38,40]. This is expected, as the mobility-related facets of

HS rate a patient's perceptions of own physical ability. Overall, HRQOL in MS and PD patients seems to be lower the more disabling, severe, and long-lasting the disease is.

In summary, exercise interventions have been found effective in improving physical ability (reducing disability) in MS and PD patients. Disability has also shown to be significantly related to patient reported HS and HRQOL, especially to the physical sub-scores of the HS/HRQOL-measures. Even so, interventions focusing on exercise and physical therapy have shown weak results in improving patient-perceived health. This suggests that relying on physical therapy alone is insufficient for achieving improvements that are meaningful to the patients. A broader, multidisciplinary approach to treatment may be necessary to positively influence quality of life in MS and PD patients, targeting social and psychological difficulties in addition to motor symptoms. A holistic treatment ideology is relevant in this approach as it emphasizes the patients' own assessment and contribution in treatment. However, effects of multidisciplinary interventions on quality of life have yet to be established [43-47], few interventions employ holistic methods, and studies on the impact of inpatient rehabilitating programs on quality of life are sorely lacking.

Expanding upon previous research, the current study has two primary objectives: First, it assesses the treatment effects of a holistic 4-week inpatient multidisciplinary intervention on physical ability and health status in patients with Parkinson's disease and patients with Multiple Sclerosis. Secondly, it explores the relationship between physical ability and self-perceived health status in these patient groups. Based on previous studies, the physical component of health status is expected to correlate with tests of physical performance. Physical test scores are expected to be of predictive value for patient-perceived physical health status, while the mental component of health status is expected to show a weaker relation to measures of physical performance.

Methods

Participants

The participant group consisted of 44 patients with Parkinson's disease and 66 patients with Multiple Sclerosis admitted to an extensive 4-week rehabilitation program in Norway. The patients were selected by the regional health authorities, through referral from each patient's regular general practitioner based on need of treatment and motivation. The participant group included 62 women and 48 men. Their age ranged from 36 to 84 years old, with a mean of 61. PD comprised the oldest patient group with a mean age of 68, while the MS patients had a mean age of 56.

Intervention

Each participant stayed at the treatment institution for 4 weeks, receiving multidisciplinary rehabilitation. The intervention emphasizes a holistic approach to treatment encouraging patients to be active agents, not passive receivers, of treatment. Accordingly, the intervention was not standardized but tailored for each individual according to goals and needs identified in collaboration with the patient. Treatment included physical- and occupational therapy, weight and balance training, as well as outdoor activities. The program also emphasizes mental health with both individual and group interventions focusing on psychoeducation, strategies for self-care and coping with the diseases, and health promotion advice. It targeted

symptoms of sleep disturbances, pain, and malnutrition. Social aspects were included, involving activities such as restaurant visits, horseback riding, hikes, board games etc. Data collection was conducted at admission and at program completion.

Measurement instruments

The patients carried out the following three physical tests aimed to measure motor function: The 6-Minute-Walk Test (6MW), which is a measure of the maximum distance a person is able to walk in 6 min. Originally a 12-min walk-run test of maximal oxygen uptake [48], the 6MW was later modified to measure sub-maximal aerobic capacity. The test has been used extensively in research, and has shown good test-retest reliability in elderly people [49-51] and patients with cardiovascular disease [52]. Construct validity has been supported through correlations with activity level in elderly people [49], and maximal oxygen consumption in a variety of patient groups [53]. In MS patients, limitations in ADL-functions, subjective fatigue and resting heart rate have been found as significant determinants for 6MW [54]. The 6MW was deemed the walk test of choice in a 2001 review [53] because of its ease of administration, correlations with ADL functions, and tolerance in patient groups with impaired motor functions. The Timed Up-and-Go (TUG) test was also used. It is a timed test of a subject's speed in standing up from an armchair, walking a distance of three meters, turning, walking back to the chair again, and sitting down. It was originally used for clinical observations of balance in elderly people, assessing risk of falling [55]. Later modified by Podsiadlo and Richardson [56], it is now a timed test used to evaluate basic mobility skills. The validity of the test has been found satisfactory through correlation of TUG scores with measurements on the Berg Balance Scale, Dynamic Gait Index, Hauser Deambulation Index, Dizziness Handicap Inventory, and Activities-specific Balance Confidence in people with MS [57]. TUG has also been deemed valid for use in people with PD, and the interrater and test-retest reliability of TUG was found to be high in this patient population [58]. The TUG test has been found to discriminate well between fallers and non-fallers in elderly subjects [51,59]. The Sit-To-Stand (STS) test was the final test used for measuring physical capability. This test is administered by measuring the number of times a person is able to stand and sit on a chair in the span of 30 seconds. It is used as a test of functional lower body strength [60], and has been shown to be a significant predictor of falls and ADL-functions in elderly people [61,62]. It has also shown significant predictive effect on mobility disability status (measured by 800m walking and climbing a flight of stairs) in elderly people [63]. The 5-repetition STS test has shown good test-retest reliability across numerous studies on older adults [64], and also been validated and found reliable amongst both PD and MS patients [65,66]. The 12-item Short-Form Health Survey (SF-12) translated to Norwegian was used to measure patient-perceived health status. The SF-12 is a self-report questionnaire measuring generic health status. The choice of health status questionnaire had to be generic because of the inclusion of two different diagnostic groups. Ware et al. [67] originally developed a 36-item questionnaire (SF-36) to capture health outcomes and disease burden from the patient point of view. It was designed to measure the eight most central concepts related to health, disease and treatment derived from the Medical Outcomes Study [67], and has become a widely used tool for measuring health status [68]. Ware et al. [69] derived 12 items from the SF-36 using regression methods, with the intent to reproduce two of the original eight constructs: the Physical Component Summary (PCS) and Mental Component Summary (MCS) scores. The SF-12 has been shown to accurately reproduce the

two summary scores PCS and MCS in the general population [69] and among various patient groups, including PD [70]. Substantial correlations between the SF-36 and SF-12 outcomes have also been found [71]. Based on symptoms cognitive impairments and fatigue being common in people with PD or MS, the SF-12 was chosen for its briefness and ease of administration. The PCS and MCS summary scores were calculated using the published algorithm [68].

Statistical analysis

To test treatment effect on physical ability, paired samples t-tests were conducted, independently comparing the results of three physical tests, 6-min walking (Walk), timed up-and-go test (TUG), and stand-sit test (Stand), before and after the intervention. Treatment effects were tested for the total patient population and for each patient group separately. The data was also split among people with low-, intermediate- and high Pre-test physical scores, and treatment effect was tested for each group separately. Similarly, paired samples t-tests

were conducted to test the treatment effect on the SF-12 outcomes on the Physical Composite Scale (PCS) and Mental Composite Scale (MCS). T-tests were also used to analyse the difference in SF-12 HS between the treatment group and the general population. To test differences in improvements on physical tests and SF-12 outcomes due to various demographics (diagnosis, age, gender), a multivariate analysis of variance (MANCOVA) was used. Bivariate correlations were analysed examining the strength of the associations between the two SF-12 outcomes (PCS and MCS) and the three physical outcome measures (6MW, TUG, STS). Multiple hierarchical regression analyses were conducted, testing the predictive value of various variables on SF-12 outcome measures.

Results

Treatment effect on physical performance

	Parkinson's disease					Multiple sclerosis				
	Before	SD	After	SD	t	Before	SD	After	SD	t
6MW	494.72	139.35	548.58	152.08	-7.35*	319.76	178.23	378.42	186.73	-8.03*
TUG	7.95	5.09	6.56	4.27	3.64*	14.24	9.88	12.1	8.46	3.54*
STS	14.33	5.87	17.21	6.35	-7.71*	9.69	4.03	12.51	5.21	-8.00*
N=43-103; *p<0.01; 6MW=6-min walk test; TUG=Timed up-and-go test; STS=Sit-to-stand test										

Table 1: Differences in physical performance before and after treatment.

The Table 1 shows the results differences in physical performance before and after treatment intervention. There were significant improvements in performance on all three tests across the two patient groups (p<0.01). Both the patient group with Parkinson's disease and the patient group with Multiple Sclerosis walked further on the 6MW test after treatment than before treatment, improving by 53.86 m (t=-7.35, p<0.01) and 58.66 m (t=-8.03, p<0.01) respectively, showing low to moderate effect sizes (Cohen's d=0.37 and d=0.32). The PD group reduced test-time on the TUG test by 1.39 sec (t=3.64, p<0.01) and the MS group reduced time by 2 sec (t=3.54, p<0.01), but the effect sizes were small (Cohen's d=0.29 and d=0.23). Both patient groups also improved on the STS test increasing the amount of times they were able to stand and sit by 2.88 (PD, t=-7.71, p<0.01) and 2.82 (MS, t=-8.00, p<0.01). This improvement was of moderate effect size (Cohen's d=0.47 and d=0.60). These results show that the treatment intervention was successful in improving the physical ability of the patients, although modest effect sizes.

For analytical purposes, the data was split into three groups according to performance on each of the physical tests before treatment. The low-performance group consisted of the patients scoring in the lower third of the population on each of the three tests separately (i.e. walked shortest on the 6MW test, completed the TUG test slowest, performed fewest repetitions on the STS test), the intermediate group placing in the middle third, and the high pre-test group scoring in the upper third of the participant population. Analyses of treatment effects show significant improvements in all three groups, on all three physical tests (p<0.01) (Table 2). On the 6MW test, the patients in the low- and high-performance groups showed a moderate improvement (Cohen's d=0.44 and Cohen's d=0.56

respectively), while the intermediate group showed a strong improvement (Cohen's d=1.56).

	Low Pre-test score			Medium Pre-test score			High Pre-test score		
	Before	After	t	Before	After	t	Before	After	t
6MW		224.45	-4.19**	418.45	500.48	-8.72**	582.71	631.7	-7.73**
TUG	20.63	17.07	3.46**	8.24	6.94	6.33**	5.33	4.84	5.42**
STS	6.23	8.81	-6.91**	10.39	13.3	-9.51**	17.15	20.16	-5.34**
N=31-38; **p < 0.01; 6MW=6-min walk test; TUG=Timed up-and-go test; ST=Sit-to-stand test									

Table 2: Differences in physical performance before and after treatment according to pre- treatment physical ability.

Similarly, the groups of low- and high-scorers on the TUG-test pre-treatment showed an improvement with moderate effect sizes (Cohen's d=0.39 and Cohen's d=0.58 respectively), and the intermediate group showed a stronger improvement (Cohen's d=1.00). The strongest increase on the STS test was shown in the intermediate group as well as well (Cohen's d=1.82), but here the low-scoring group showed an increase with strong effect size (Cohen's d=1.16) and the high-scorers improved moderately/strongly (Cohen's d=0.60).

Upon further inspection, a significant difference in improvement on the 6MW test between the three groups arranged by Pre-test 6MW score was found (F $(2.95)=6.48$, $p<0.01$). A Tukey post hoc test revealed that the improvements in 6MW distance was significantly lower among the high-scoring group (49.06 ± 37.0, $p<0.05$) and the low-scoring group (40.33 ± 55.3, $p<0.01$) compared to the intermediate group (82.03 ± 52.4). No significant differences were found in STS improvements among the low-, medium- and high-scoring Pre-test STS groups ($F(2.99)=0.25$, $p=NS$). However, a one-way ANOVA revealed a statistically significant difference in TUG improvements between the three groups arranged by Pre-test TUG results ($F(2.100)=6.40$, $p<0.01$). Here, a Tukey post hoc test revealed that the group with the poorest TUG performance before treatment improved more (3.56 ± 6.2) than both the high-functioning (0.49 ± 0.5, $p<0.01$) and medium-functioning groups (1.30 ± 1.2, $p<0.05$). No significant difference was observed between the medium- and high-scoring groups. These results show that high, moderate and low functioning patients benefit from the treatment program. However, the magnitude of the improvement seems to differ among the various groups and tests.

Treatment effect on health status (SF-12)

Table 3 shows changes in SF-12 scores between pre-treatment and post-treatment measurements. There were significant improvements on both the mental and physical composite scores of SF-12 (MCS and PCS) across patient groups. The total participant group showed improvement on PCS from 36.56 to 42.49, $t(71)=6.55$ $p<0.05$, with a moderate effect size (Cohen's $d=0.68$). There were improvements on MCS from 46.55 to 55.38; $t(71)=7.46$ $p<0.05$, with a strong effect size (Cohen's $d=0.88$). The patient group diagnosed with PD improved on both reported PCS; $t(32)=3.20$ $p<0.05$, and MCS; $t(32)=3.93$ $p<0.05$,

with moderate effect sizes (Cohen's $d=0.47$ and 0.74 respectively). The MS group improved on both facets of SF-12 HS; $t(38)=6.05$ $p<0.05$ (PCS), and $t(38)=6.62$ $p<0.05$ (MCS) with strong effect sizes (Cohen's $d=0.89$ and 0.99).

	Total (N=72)			PD (N=33)			MS (N=39)		
	Before	After	t	Before	After	t	Before	After	t
PCS	36.56	42.49	-6.55**	40.42	44.15	-3.20**	33.3	41.09	-6.05**
MCS	46.55	55.38	-7.46**	47.92	54.51	-3.93**	45.39	56.12	-6.62**

**p<0.01; PCS=SF-12 Physical composite score; MCS=SF-12 Mental composite score

Table 3: Differences in SF-12 health status before and after treatment.

When divided into two age groups, 35-59 and 60-85 years of age, significant improvements in SF-12 HS were observed in both groups. The younger patients showed improvements on both PCS ($t(40)=-5.10$, $p<0.01$) and MCS ($t(40)=-6.33$, $p<0.01$) and these improvements were strong (Cohen's $d=0.87$ and Cohen's $d=0.89$ respectively). Older patients improved moderately on PCS ($t(30)=-2.95$, $p<0.01$, Cohen's $d=0.43$) and strongly on the MCS facet of SF-12 QOL ($t(30)=-4.35$, $p<0.01$, Cohen's $d=0.86$). These results show that both diagnostic groups and age groups reported improved HS measured by SF-12, with moderate to strong effect sizes.

Group differences in physical performance

	Diagnosis			Age			Gender		
	PD	MS	F-value	35-59	60-85	F-value	Female	Male	F-value
Pre 6MW	494.72	323.7	26.98**	372.51	421.02	1.3	372.57	433.35	0.35
Pre TUG	7.95	12.99	13.87**	10.85	10.68	1.4	11.01	10.43	0.12
Pre STS	14.33	9.96	20.64**	11.92	11.87	8.50**	10.17	14.06	10.23**
Post 6MW	548.58	382.46	25.55**	440.42	468.59	2.58	433.02	485.09	0.17
Post TUG	6.56	11.49	13.55**	9.07	9.49	2.19	9.89	8.57	0.01
Post STS	17.21	12.82	16.36**	14.98	14.59	6.90**	13.11	16.84	7.22**

*p<0.05; **p<0.01; Wilks λ=0.740**; Wilks λ=0.879; Wilks λ=0.825*; PCS=SF-12 physical composite score; MCS=SF-12 Mental composite score

Table 4: Differences in physical performance among demographic groups.

Table 4 shows differences in physical performance between different patient groups, age groups and gender, comparing test results for the different demographic groups both before- and after treatment. An overall difference on physical scores was found between patients with Parkinson's disease and Multiple Sclerosis (Wilks λ=0.740, $p<0.01$). More specifically, PD patients walked further on the 6-min walk test, achieved faster times on the Timed Up-and-Go test and managed more repetitions of standing and sitting on the Stand-to-Sit than MS patients both before treatment and after treatment ($p<0.01$). No significant difference was found between age groups on physical ability, but there

was an overall difference between the two genders (Wilks λ=0.825, $p<0.05$). Male participants performed significantly better than female participants on the STS test both before and after treatment ($F(1.89)=10.23$, $p<0.01$ and $F(1.89)=7.22$, $p<0.05$ respectively). However, no such gender difference was observed on the 6MW or the TUG test. No statistically significant interaction effects were observed between any combinations of the independent variable.

Group differences in health status

	Parkinson	MS	F-value
Pre-test PCS	40.42	33.3	12.30**
Pre-test MCS	47.92	45.39	0.67
Post-test PCS	44.15	41.1	5.54*
Post-test MCS	54.51	56.12	1.22

N=33-39; *p<0.05; **p<0.01; Wilks λ=0.791**; PCS=SF-12 physical composite score; MCS=SF-12 mental composite score

Table 5: Differences in SF-12 health status between Parkinson's and MS patients.

Differences in measures of SF-12 quality of life between PD and MS patients are shown in (Table 5). There was an overall significant difference between the patients with PD and patients with MS in SF-12 HS (Wilks λ=0.791 p<0.01). PD patients received significantly higher Physical Composite Scores than the MS group before treatment, with a score of 40.42 compared to 33.30 (F(4.65)=12.30 p<0.01), a difference of 7.12 points on a scale from 1-100. A significant difference in PCS is maintained post treatment with PD patients scoring 44.15 and MS patients scoring 41.10 (F(4.65)=5.54 p<0.05), a difference of 3.05 points. For the Mental Composite Score, no significant difference was found between the two patient groups.

Comparing physical ability to self-perceived health status

	Pre PCS	Pre MCS		Post PCS	Post MCS
Pre 6MW	0.48**	0.03	Post 6MW	0.44**	-0.24*
Pre TUG	-0.43**	0.04	Post TUG	-0.32**	0.29**
Pre STS	0.40**	0.24*	Post STS	0.28**	-0.03

N=75-103; *p<0.05; **p<0.01; Reported values are Pearson's r. 6MW=6-min walking test; TUG=Timed up-and-go test; STS=Stand-to-sit test; PCS=SF-12 physical composite score; MCS=SF-12 mental composite score

Table 6: Associations between physical performance and health status.

Table 6 shows the associations between Physical Composite Score of SF-12 (PCS) and the three measures of physical performance both before and after treatment. Individuals scoring higher on PCS walked further in the 6MW test (r=0.48, p<0.01 before, and r=0.44, p<0.01 after), achieved a faster time on the TUG test (r=-0.43, p<0.01 before and r=-0.44, p<0.01 after), and performed better on the STS test (r=0.40, p<0.01 before, and r=0.28, p<0.01 after). The correlations of the Mental Composite Score of SF-12 (MCS) were less clear-cut. Before treatment, individuals scoring higher on MCS performed significantly better in the STS (r=0.24, p<0.05), but the Pre-test MCS score showed no relationship with the other two physical tests. After treatment, no correlation was found between MCS and the STS, but higher MCS was significantly related to worse performance on both the 6MW (r=-0.24, p<0.05) and a slower TUG time (0.29, p<0.01).

Regression analysis (Table 7) was conducted testing the predictive value of demographic variables and measures of physical performance on patient perceived health status. As shown in the table a total of four regression analyses were carried out. In model one, diagnosis, gender

and age group was found to contribute significantly to the regression model for PCS before treatment (F(3.70)=4.36, p<0.05), and accounted for 16% of the variation in PCS. According to the regression analysis only diagnostic group had a significant unique predictive effect (β=-0.35, p<0.05). Adding physical test scores increased the predictive value of model 2, explaining an additional 11% of the variance in physical HS and this change in R² was significant (F(3.67)=3.30, p<0.05).

Model1		Pre-test PCS		Pre-test MCS		Post-test PCS		Post-test MCS	
		β	t	β	t	β	t	β	t
	Diagnosis	-0.31	-2.33*	-0.24	-1.7	-0.3	-2.27*	0.28	2.10*
	Gender	0.19	1.58	0.04	0.33	-0.05	-0.38	0.14	1.16
	Age	-0.04	-0.34	-0.1	-0.73	-0.2	-1.64	0.12	0.98
	R²	0.16		0.05		0.06		0.05	
	F	4.36**		1.2		1.91		1.57	
Model2	**Diagnosis**	-0.1	-0.68	1.2	-1.55	-0.03	-0.24	0.17	1.15
	Gender	0.19	1.49	-0.11	-0.78	-0.02	-0.18	0.05	0.41
	Age	-0.02	-0.14	-0.04	-0.26	-0.11	-0.87	0.12	0.94
	Pre-test 6MW	0.29	1.45	-0.28	-1.27				
	Post-test 6MW					0.48	2.61	-0.34	-1.76
	Pre-test TUG	-0.11	-0.67	0.11	0.59				
	Post-test TUG					0.01	0.08	0.16	1.03
	Pre-test STS	-0.01	-0.04	0.47	2.5				
	Post-test STS					-0.06	-0.38	0.38	2.47*
	R²	0.27		0.13		0.21		0.15	
	R² change	0.11		0.08		0.14		0.1	
	F change	3.30*		2.17		4.79**		3.21*	

Pre-test N=74; Post-test N=88; **p<0.01; *p<0.05; 6MW=6 min walking test; TUG=Timed-up-and-go test; STS=Stand-sit test; PCS=SF-12 physical composite score; MCS=SF-12 mental composite score

Table 7: Regression models predicting health status with demographic variables and physical performance.

Analysing the post-test data, only model two contributed significantly to the regression equation, and it was predictive of both PCS (F(6.81)=3.47, p<0.01) and the mental component of HS (MCS) (F(6.81)=2.45, p<0.05), explaining 21% (physical test scores contributing to 14%) of the variance in PCS and 15% (physical test scores contributing 10%) of the variance in MCS. Diagnosis had a

significant unique predictive effect on both PCS (β=-0.30, p<0.05) and MCS (β=-0.38, p<0.05), but the performance on the STS also had a unique predictive effect on MCS (β=-0.38, p<0.05).

In summary, the physical test scores included in model two seem to be important predictors of SF-12 HS, with greater contributions towards predicting PCS than MCS.

			N	B	Hazard ratio	95.0% CI for Exp (B)	
						Lower	Upper
Pre-test 6MW score	Post-test PCS	Low	30	1.26	3.54**	1.84	6.8
		Medium	30	0.44	1.56	0.92	2.64
		High'	29				
	Post-test MCS	Low	30	-0.59	0.55	0.28	1.11
		Medium	30	0.36	1.43	0.81	2.54
		High'	29				
Pre-test TUG score	Post-test PCS	Low	32	1	2.72**	1.5	4.93
		Medium	31	0.32	1.38	0.79	2.41
		High'	30				
	Post-test MCS	Low	32	-0.45	0.64	0.31	1.3
		Medium	31	0.24	1.27	0.72	2.25
		High'	30				
Pre-test STS score	Post-test PCS	Low	28	0.97	2.63**	1.43	4.83
		Medium	29	-0.19	0.83	0.47	1.46
		High'	35				
	Post-test MCS	Low	28	-0.28	0.76	0.39	1.49
		Medium	29	0.43	1.54	0.88	2.7
		High'	35				

*p<0.05; **p<0.01; The high scoring groups were used as reference groups for the analysis; 6MW=6 min walking test; TUG=Timed-up-and-go test; STS=Stand-sit test; PCS=SF-12 physical composite score; MCS=SF-12 mental composite score

Table 8: Pre-test physical covariates related to post-test SF-12 health status.

Table 8 shows the effects of pre-test physical covariates on Post-test SF-12 HS scores. The patients were arranged into three groups based on physical ability on each of the three physical tests before treatment. Differences in HS between the groups were then examined. The results show significant differences in post-test PCS between the groups on all three physical tests. The probability of still improving Post-test PCS at time x [P(X>x)] was significantly lower among those with low pre-test 6MW performance than the group scoring high on the 6MW test before treatment (HR=3.54, p<0.01). The low-scoring TUG-test group also showed a lower chance of still improving Post-test PCS at time x [P(X>x)] then the high-scoring group (HR=2.72, p<0.01) Similar results were found on the groups based on Pre-test STS score. Low-

performers showed significantly lower probability of scoring high on PCS after treatment, than the high-performing STS group (HR=2.63, p<0.01).

There are no associations between Pre-test physical performance and Post-test MCS were found. However, survival analyses of MCS difference scores (i.e. change from Pre-test to Post-test MCS) showed that the patients in the lower half of Pre-test physical performance displayed a greater chance of improving MCS at time x [P(X>x)] than the upper half of physical performers. This difference was significant for the TUG test group (HR=0.36, p<0.05, appendix figure A9) and the STS group (HR=0.30, p<0.01), but not for the groups based on Pre-test 6MW-performance.

			N	B	Hazard ratio	95.0% CI for Exp (B)	
						Lower	Upper
Pre-test 6MW score	Post-test PCS	Low	29	1.28	3.60**	1.8	7.19
		Medium	31	0.55	1.73	0.99	3.05
		High'	28				
	Post-test MCS	Low	29	-0.31	0.73	0.37	1.47
		Medium	31	0.37	1.44	0.82	2.53
		High'	28				
Pre-test TUG score	Post-test PCS	Low	29	0.7	2.02*	1.06	3.87
		Medium	31	0.32	1.38	0.81	2.33
		High'	32				
	Post-test MCS	Low	29	-0.56	0.57	0.3	1.11
		Medium	31	0.14	1.15	0.65	2.02
		High'	32				
Pre-test STS score	Post-test PCS	Low	39	0.72	2.06*	1.16	3.65
		Medium	27	-0.17	0.84	0.47	1.51
		High'	26				
	Post-test MCS	Low	39	0.19	1.21	0.62	2.36
		Medium	27	0.37	1.44	0.8	2.6
		High'	26				

*p < 0.05; **p < 0.01; The high scoring groups were used as reference groups for the analysis; 6MW=6 min walking test; TUG=Timed-up-and-go test; STS=Stand-sit test; PCS=SF-12 physical composite score; MCS=SF-12 mental composite score

Table 9: Post-test physical covariates related to post-test health status.

In (Table 9) associations between post-test physical performance and health status after treatment are displayed. As in the previous analysis, the patients were arranged into groups based on physical ability, but this time Post-test score was the deciding factor for the groups. These results also showed that the low-scoring groups had a lower probability of still improving Post-test PCS at time x [P(X>x)] than the high-performance groups for all three tests; 6MW (HR=3.60,

$p < 0.01$), TUG (HR=0.02, $p < 0.05$), and STS (HR=2.06, $p < 0.05$). No significant associations were found between Post-test physical group and Post-test MCS score. When compared to change in MCS, however, the lower half of STS scorers after treatment displayed a larger

improvement of MCS (HR=0.32, $p < 0.01$). This association was not found in the 6MW and TUG groups.

Comparing PD and MS patients to US norms

Age		Treatment population			US norms					
		Mean	SD	N	Mean	SD	N	Diff	t	Cohen's d
35-44	PCS	43.24	8.04	6	52.18	7.3	487	-8.94	2.98**	1.16
	MCS	46.11	13.44		50.1	8.62		-3.99	1.12	
45-54	PCS	42.95	8.73	23	49.71	9.5	324	-6.76	3.31**	0.74
	MCS	54.62	9.61		50.45	9.55		4.17	2.02*	0.43
55-64	PCS	42.63	8	28	46.55	10.63	250	-3.92	1.89	
	MCS	58.23	7.71		50.57	9.82		7.66	3.99**	0.87
65-74	PCS	43.49	8.46	29	43.65	11.02	408	-0.16	0.08	
	MCS	55.46	9.21		52.1	9.53		3.36	1.84	
75-95	PCS	37.3	6.83	12	38.68	11.04	217	-1.38	0.43	
	MCS	55.21	9.43		50.06	10.94		5.15	1.6	
Total	PCS	42.34	8.25	98	50.12	9.45	2329	-7.78	8.02**	0.88
	MCS	55.45	9.44		50.04	9.59		5.41	5.47**	0.57

*$p < 0.05$; **$p < 0.01$; PCS=SF-12 Physical Composite Score; MCS=SF-12 Mental Composite Score

Table 10: Differences in health status between patient group post treatment and US norms.

Table 10 shows differences in health status, measured by the SF-12 facets PCS and MCS, between treatment population after intervention and US norms. Examining the data including all age groups, the treatment population showed significantly lower PCS than the US norm ($t(2328)=-7.78$, $p < 0.01$) and this difference was large (Cohen's d=0.88). There was also a significant difference in MCS between the two groups, but surprisingly this difference favoured the treatment group. They showed higher MCS post treatment than the US norm ($t(2328)=5.47$, $p < 0.01$) with a moderate effect size (Cohen's d=0.57) (Table 10).

Distinguishing between age groups the data shows a more nuanced picture. PCS is only significantly different among the two youngest age groups from 35-45 and 45-54 years old. This part of the patient population showed lower PCS than US norms ($p < 0.01$), with strong effect sizes (Cohen's d=1.16 and d=0.74 respectively). No such difference was found for the population over 55 years of age. For the MCS data only the patients of age between 45-54 and 55-64 showed significantly higher scores than US norms ($p < 0.05$; $p < 0.01$). Effect sizes here were moderate for ages 45- 54 (Cohen's d=0.43) and strong for ages 55-64 (Cohen's d=0.87). Overall these results indicate that older patients with PD or MS experience similar perceived health status to the US norm population, while younger patients experience lower physical HS than norms, but may experience better mental HS.

Discussion and Conclusion

Positive changes in both physical and mental health status indicate that patient-perceived health status is changeable through treatment

intervention. Previous studies examining the effects of general interventions on health status and health-related quality of life among these patient groups indicate only small improvements [25,28,43,45,72]. Moderate PCS- and large MCS improvements in this study were therefore not expected. These improvements show that patients perceive their own health as better after treatment, both physically and psychologically.

Few previous studies have explored the effects of short, intensive, inpatient treatment programs on quality of life measures in these patient groups. Results of the current study suggest that the short intensive inpatient rehabilitation is effective in producing short term improvements. The MDI programs studied in the literature vary in focus, duration, frequency, intensity etc. Knowing the heterogeneity of MS and PD patients regarding symptoms and disability, finding an 'ideal' intervention across patients is nearly impossible [73]. This variation within the patient groups makes studying mechanisms of change, or pathways leading to improvements in quality of life, difficult. Two plausible mechanisms are proposed: First, improvements on the level of physical function may influence HS positively. Secondly, the holistic, multidisciplinary approach to treatment may target non-motor factors important to patient-perceived HS.

Supporting the first mechanism, physical ability/disability was found to be significant related to physical health status, and this is supported by previous research [35,38-40,43,74]. The regression- and correlational results were similar in magnitude to the findings of previous studies [40,41], supporting the growing body of evidence for the relationship between objective physical ability and self-perceived

physical health. Mobility and motor functions play an important role in perceived physical health status for MS and PD patients. However, the modest magnitude of these relations indicates that other factors are important to perceived health. There is considerable discrepancy between subjective and objective measurements of health. Theoretically, physical health status is the most proximal patient-reported outcome measure to physical ability. Both health-related quality of life and global quality of life are more distal constructs. Even so, most of the variance in perceived physical health was explained by other factors than physical test scores, showing the importance of non-motor factors. This is further highlighted by the divergent, inconclusive results for the relationship between mental health status and physical ability, supporting the model of mental health as a construct more distant from physical function. Although physical ability affects HS, the increase in both physical and mental components of HS seen in the current study must also be affected by changes in factors not related to physical disability. The observation of HS changes exceeding the improvements in physical ability gives credence to the second proposed mechanism of critical non-motor factors being affected by the intervention.

Numerous previous studies have explored the effects of individual symptoms on quality of life in MS and PD patients, identifying depressive symptoms as one of the strongest links to decreases in HS/HRQOL [6,16,73,74]. Other variables related to HS/HRQOL in these patient groups are psychosocial functioning [75], fatigue [76], and emotional adjustment to illness [77]. There is support for some effect of exercise improving depressive symptoms in the general population [74], and the effect has found specifically in MS patients [78]. The effects of exercise on fatigue are limited but may indicate a small improvement [24,25]. Knowing the high incidence and large impact of depression and fatigue in these patient groups, and the central role of psychosocial functioning and emotional adjustment in quality of life outcomes, targeting these symptoms specifically through multidisciplinary treatments is crucial.

The holistic approach to rehabilitation, emphasizing the patients' own experiences, values and goals, may be important in improving quality of life. Storr et al. [72] randomised controlled trial assessed an inpatient intervention of similar duration (3-5 weeks) to the current study but found no difference in QOL measures between treatment group and controls. Although the studies differ in research design, one unique trait of the current intervention compared to the intervention of Storr et al. [72] study is the holistic ideology. An explicit focus on patient-driven treatment is a differentiating factor that could be important in producing effects at the level of patient reported outcomes.

Corresponding with previous research, both patient groups showed improvements in physical ability. However, the effects of the current intervention were low to moderate in size. The characteristics of the physical therapy provided in treatment corresponded well to those identified as important for short interventions in Latimer-Chang et al. [25] systematic review; a high frequency (3 times per week or more) and supervision during training. This indicates that other factors may have contributed to the modest results. Primarily, the short duration of 4-weeks for an intervention aimed at improved motor function is thought to be a factor. Also, the large variance in physical function within the patient groups is a statistical factor yielding lower effect sizes. High standard deviation is expected in patient groups of progressive neurodegenerative diseases where the severity of the motor symptoms vary greatly from early- to late stages of the diseases.

The short-term gains found are uplifting, but due to the lack of follow-up data long-term effects are unknown. Frazzita et al. [79] study on a 4-week intensive rehabilitation for PD patients suggests good effects countering loss of ADL-functions and physical ability up to one year after intervention. However, further research is needed to explore the stability of improvements in physical function and quality of life over time. Also, inpatient rehabilitation is an expensive intervention. Analyses of the cost-effectiveness of such programs are needed for a discussion on treatment choices for MS and PD patients.

Some differences among the two patient groups of the study were found, both in health and treatment response. PD patients performed better physically, and reported better physical health status than MS patients, both before and after treatment, despite the fact that MS patients on average were younger. MS patients showed a larger improvement in mental health over the course of the treatment. These findings are in accordance with a previous study, where people with MS generally reported poorer physical health, but better mental health than people with PD [80]. The disparity in physical ability between the patient groups is likely due to the different nature of the diseases' impact on motor function. The difference in mental health benefits of the program may need further study.

Contrary to the chronic progressive degenerative nature of the diseases, age was not found to be a significant factor for either physical ability or HS. This was surprising. Previous studies have identified time since diagnosis as a significant predictor for disability and HS/HRQOL in both PD and MS patients [36,37,42]. The lack of difference found in the current study could be explained the differences between the diagnostic groups. The PD patients were on average older than MS patients, but the PD patients generally performed better physically and rated their physical health higher. Factors differentiating the treatment response between the two patient groups should be investigated in future research.

The best predictor of physical ability and health at program completion was physical ability and health before the intervention, and this was expected. Differences in treatment responses among low-, intermediate- and high functioning patients showed ambiguous results. For some tests, the group with the largest physical disabilities showed the greatest improvements (TUG, SF-12 MCS-score), for another the intermediate scorers showed the best improvements (6MW). The mechanisms behind these discrepancies are unclear and the results may be skewed by a difference in function and treatment effects between the two diagnostic groups. Smaller improvements among patients with good pre-test function could be explained by a ceiling effect, where improvements stagnate when approaching an upper bound of function and health in these diagnostic groups. The high-functioning patients could also have been having a healthier lifestyle, more closely resembling that of the rehabilitation conditions, before the intervention. The program and staff could have been better suited for, or spend more resources on, the more disabled patients leading to larger effects for this group. Possible advantages for the intermediate pre-treatment group on 6MW improvements may be good enough function to participate in activities and recover from exercise, while still having room for improvement. Differences in improvements among the tests may indicate a difference in the tests ability to distinguish between function as results deviate from the norm. This shows the necessity of including multiple tests of physical ability in a study. The ability to profit from treatment depending on diagnosis or disability is difficult to discern in a study with multiple interaction effects between disease, motor function, HS and

individualized treatment. Randomized, controlled studies exploring fewer variables are needed to identify specific factors leading to positive changes.

The treatment population rated their physical health status much lower than US norms. This result was expected and supports earlier findings on the impact of these diseases on physical health status [75, 80]. However, the mental health status reported by patients after treatment was significantly better than US-norms. This was unexpected. When interpreting this result, Nortvedt et al. [81] study on MS patients' responses on SF-12 is relevant. They found that the SF-12 questionnaire tended to overestimate mental health (MCS) in MS patients. The authors attributed this overestimation to the orthogonal factor rotation used to calculate the PCS and MCS factors (i.e. to differentiate between the two components, some factors loading positively on PCS load negatively on MCS, and vice versa). Poor ratings on the PCS facet (seen in treatment population) may therefore affect the MCS measurement positively. This must be considered when reviewing the positive results on perceived mental health. Indications that the treatment population perceive their disease's impact on physical health as greater than mental health are interpreted with caution.

Examining specific age groups, PCS was only significantly worse among the younger patients. Again, this may be due to MS patients comprising a large percentage of the younger participants, as this diagnostic groups showed the lowest PCS. The middle age groups (45-64) showed highest MCS compared to norms. A young age of onset may have higher impact on HS, being especially taxing as it is chronic, progressive, without good treatments [6]. Differences in HS were not found in patients older than 65 years of age. This may be due to PCS decreasing with increasing age in the norm population, indicating an increase in physical limitations among older people.

The current study used a pre-test-post-test design, and the lack of a control condition makes the results susceptible to confounding placebo effects or patient/caregiver expectations. Even though MS and PD are progressive diseases with expected increase in disability over time, QOL outcomes may be over-estimated in non-experimental conditions. A meta-analysis by Motl and Gosney [10] found no significant differences in effect sizes of HS/HRQOL improvements between experimental and non-experimental designs, but results showed a tendency of overestimation when no control condition was included. Considering the strong treatment effects of the study, a possible overestimation does not alter the positive conclusion.

No follow-up data was included in this study. Conclusions can therefore only be drawn for effects in the short-term. Also, selection bias needs to be considered in this study. Patients participating in program were motivated for treatment, and a doctor's referral was needed to attend the program, attesting to a need for rehabilitation. There was no "blindness" among staff or patients regarding data collection or goals of the intervention. The collection of data was a part of rehabilitation routines at the institution, and both caregivers and patients knew that Post-test results would be compared to results at entry.

The inclusion of two different diagnostic groups in the study necessitated the use of a generic QOL measure. Comparing generic and specific measures, Motl and Gosney [10] found that MS-specific measures of QOL were generally associated with larger effects. Disease-specific instruments have also been recommended for PD patients. A cross-sectional study has contradicted this, finding no difference between generic and disease-specific measures in same group of MS patients [22]. The use of a generic tool may have contributed to underestimations of effects. The inclusion of disease-specific measures as an addition to the generic measure would have given the results increased validity. Also, health status measures (including SF-12) focus on limitations/negative experiences, bringing adverse symptoms to the foreground. Quality of life questionnaires focusing on positive experiences, personal resources and protective factors could expose important favourable traits in the patient population. A combination of generic and specific instruments, as well as both proximal and distal QOL-measures would provide a broader foundation for conclusion but would be more taxing for the patients to complete, and it would increase the scope of the study considerably.

As previously noted, the orthogonal factor rotation used in differentiating between the physical and mental composite scores of the SF-12 is a methodological issue, especially for patients showing large discrepancies between physical and mental health. Caution is therefore advised in accentuating the high MCS seen in this patient group. The overestimation is expected to be lower for PD patients as this group reported better physical health status.

Despite methodological challenges there is still a solid foundation for conclusion. The study analyses changes of the measured variables from beginning to the end of the 4 week rehabilitation. Due to the progressive nature of PD and MS, spontaneous improvement in disability and QOL is not expected as time progresses. Although the study does not control for placebo effects, the treatment effect found is of such magnitude that a positive conclusion should be reported. Due to the lack of follow-up data, conclusion is limited to short term effects.

In summary, inpatient, multidisciplinary treatment was found to be an effective intervention for multiple sclerosis and Parkinson's disease patients, improving both physical and mental health in the short term. Physical ability seems to be an important factor for patient-perceived physical health, but not for mental health status. Quality of life outcomes for these patients rely on both motor and non-motor factors, implying a need for broad interventions. The results of the current study support a holistic, multidisciplinary approach to treatment of MS and PD, but follow-up data is needed to support long-term effect.

References

1. Compston A, Coles A (2002) Multiple Sclerosis. Lancet 359: 1221-1231.
2. Berardelli A, Rothwell JC, Thompson PD, Hallett M (2001) Pathophysiology of bradykinesia in Parkinson's disease. Brain 124: 2131-2146.
3. Pagonabarraga J (2016) Parkinson's disease: Definition, diagnosis and management. Encyclopedia of Movement Disorders 405-412.
4. Chaudhuri KR, Healy DG, Schapira AH (2006) Non-motor symptoms of Parkinson's disease: Diagnosis and management. Lancet Neurol 5: 235-245.
5. Herlofson K, Lie SA, Årsland D, Larsen JP (2004) Mortality and Parkinson disease A community based study. Neurol 62: 937-942.
6. Benito-Leon J, Morales JM, Rivera-Navarro J, Mitchell AJ (2003) A review about the impact of multiple sclerosis on health-related quality of life. Disabil Rehabil 25: 1291-1303.
7. Martinez-Martin P (1998) An introduction to the concept of "quality of life in Parkinson's Disease". J of Neurol 245: 2-6.
8. Pavot W, Diener E (1993) Review of the Satisfaction With Life Scale. Psychological Assessment 5: 164-172.
9. Rejeski WJ, Mihalko SL (2001) Physical Activity and Quality of Life in Older Adults. J Gerontol A Biol Sci Med Sci A 56: 23-35.

10. Motl RW, Gosney JL (2008) Effect of exercise training on quality of life in multiple sclerosis: A meta-analysis. Mult Scler 14: 129-135.

11. WHOQOL Group (1995) The World Health Organization quality of life assessment (WHOQOL): Position paper from the World Health Organization. Soc Sci Med 41: 1403-1409.

12. Speight J, Reaney MD, Barnard KD (2009) Not all roads lead to Rome - a review of quality of life measurement in adults with diabetes. Send to

13. Diabet Med 26: 315-327.

14. Guyatt GH, Feeny DH, Patrick DL (1993) Measuring health-related quality of life. Annals of Internal Medicine 118: 622-629.

15. Anderson KL, Burckhardt CS (1999) Conceptualization and measurement of quality of life as an outcome variable for health care intervention and research. J Adv Nurs 29: 298-306.

16. Den Oudsten BL, Van Heck GL, De Vries J (2007) Quality of life and related concepts in Parkinson's disease: A systematic review. Mov Disord 22: 1528-1537.

17. De Vries J (2001) Quality of Life Assessment. In: A.J.J.M. Vingerhoets (Ed.), Assessment in behavioural medicine (353-370). Hove, UK: Brunner Routledge.

18. Moons P (2004) Why call it health-related quality of life when you mean perceived health status? Eur J Cardiovasc Nurs 3: 275-277.

19. Martinez-Martin P, Kurtis MM (2013) Health-related quality of life as an outcome variable in Parkinson's disease. Ther Adv Neurol Disord 5: 105-117.

20. Moons P, Budts W, De Geest S (2006) Critique on the conceptualisation of quality of life: a review and evaluation of different conceptual approaches. Int J Nurs Stud 43: 891-901.

21. Bradley C (2001) Importance of differentiating health status from quality of life. The Lancet 357: 7-8.

22. Motl RW, McAuley E, Snook EN, Gliottoni RC (2008) Does the relationship between physical activity and quality of life differ based on generic versus disease-targeted instruments? Ann Behav Med 36: 93-99.

23. McAuley E, Konopack JF, Motl RW, Morris KS, Doerksen SE, et al. (2006) Physical activity and quality of life in older adults: Influence of health status and self-efficacy. Ann Behav Med 31: 99-103.

24. Khan F, Amatya B (2017) Rehabilitation in multiple sclerosis: A systematic review of systematic reviews. Arch Phys Med Rehabil 98: 353-367.

25. Latimer-Cheung AE, Pilutti LA, Hicks A, Martin Ginnis KA, et al., (2013) Effects of exercise training on fitness, mobility, fatigue and health-related quality of life among adults with multiple sclerosis: A systematic review to inform guideline development. Arch Phys Med Rehabil 94: 1800-1828.

26. Snook EM, Motl RW (2009) Effect of exercise training on walking mobility in multiple sclerosis: A meta-analysis. Neurorehabil Neural Repair 23: 108-116.

27. Platta ME, Ensari I, Motl RW, Pilutti LA (2016) Effect of exercise training on fitness in multiple sclerosis: A meta-analysis. Arch Phys Med Rehabil 97: 1564-1572.

28. Goodwin VA, Richards SH, Taylor RS, Taylor AH, Campbell JL (2008) The effectiveness of exercise interventions for people with Parkinson's disease: A systematic review and meta-analysis. Mov Disord 23: 631-640.

29. Shen X, Wong-Yu ISK, Mak MKY (2016) Effects of exercise on falls, balance, and gait ability in Parkinson's disease – a meta-analysis. Neurorehabil Neural Repair 30: 512-527.

30. Smith KW, Avis NE, Assmann SF (1999) Distinguishing between quality of life and health status in quality of life research: a meta-analysis. Qual Life Res 8: 447-459.

31. Ellis T, de Goede CJ, Feldman RG, Wolters EC, Kwakkel G, et al. (2005) Efficacy of a physical therapy program in patients with Parkinson's disease: A randomized controlled trial. Arch Phys Med Rehabil 86: 626-632.

32. Schmitz-Hübsch T, Pyfer D, Kielwein K, Fimmers R, Klockgether T, et al. (2006) Qigong exercise for the symptoms of Parkinson's disease: a randomized, controlled pilot study. Mov Disord 21: 543-548.

33. Burini D, Farabollini B, Iacucci S, Rimatori C, Riccardi G, et al. (2006) A randomised controlled cross-over trial of aerobic training versus Qigong in advanced Parkinson's disease. Eura Medicophys 42: 231-238.

34. Ashburn A, Fazakarley L, Ballinger C, Pickering R, McLellan LD, et al. (2007) A randomized controlled trial of a home based exercise programme to reduce the risk of falling among people with Parkinson's disease. J Neurol Neurosurg Psychiatry 78: 678-684.

35. Henriksson F, Fredrikson S, Masterman T, Jönsson B (2001) Costs, quality of life and disease severity in multiple sclerosis: a cross-sectional study in Sweden. Eur J Neurol 8: 27-35.

36. Benito-León J, Morales JM, Rivera-Navarro J (2002) Health-related quality of life and its relationship to cognitive and emotional functioning in multiple sclerosis patients. Eur J Neurol 9: 497-502.

37. Pfennings L, Cohen L, Adèr H, Polman C, Lankhorst G, et al. (1999) Exploring differences between subgroups of multiple sclerosis patients in health-related quality of life. Eur J Neurol 246: 587-591.

38. Josiah AF, Gruber-Baldini AL, Anderson KE, Fishman PS, Weiner WJ, et al. (2012) The effects of gait impairment with and without freezing of gait in Parkinson's disease. Parkinsonism Relat Disord 18: 239–242.

39. Tu X, Hwang W, Hsu S, Ma H (2017) Responsiveness of the short-form health survey and the Parkinson's disease questionnaire in patients with Parkinson's disease. Health Qual Life Outcomes 15: 75-82.

40. Ellis T, Cavanaugh JT, Earhart GM, Ford MP, Foreman KB, et al. (2011) Which measures of physical function and motor impairment best predict quality of life in Parkinson's disease? Parkinsonism Relat Disord 17: 693–697.

41. Nutt JG, Siderowf AD, Guttman M, Schmidt PN, Zamudio JI, et al. (2014) Mobility, mood and site of care impact health related quality of life in Parkinson's disease. Parkinsonism Relat Disord 20: 274–279.

42. Soh SE, McGinley JL, Watts JJ, Iansek R, Murphy AT, et al. (2013) Determinants of health-related quality of life in people with Parkinson's disease: a path analysis. Qual Life Res 22: 1543-1553.

43. Khan F, Turner-Stokes L, Ng L, Kilpatrick T, Amatya B (2007) Multidisciplinary rehabilitation for adults with multiple sclerosis. Cochrane Database Syst Rev.

44. Khan F, Pallant JF, Brand C, Kilpatrick TJ (2008) Effectiveness of rehabilitation intervention in persons with multiple sclerosis: a randomised controlled trial. J Neurol Neurosurg Psychiatry 79: 1230-1235.

45. Van der Marck MA, Kalf JG, Sturkenboom IH, Nijkrake MJ, Munneke M, et al. (2009) Multidisciplinary care for patients with Parkinson's disease. Parkinsonism Relat Disord 15: 219-223.

46. Van der Marck MA, Bloem BR, Borm GF, Overeem S, Munneke M, et al. (2013a) Effectiveness of multidisciplinary care for Parkinson's disease: a randomized, controlled trial. Mov Disord 28: 605-611.

47. Van der Marck MA, Munneke M, Mulleners W, Hoogerwaard EM, Borm GF (2013b) Integrated multidisciplinary care in Parkinson's disease: a non-randomised, controlled trial (IMPACT). Lancet Neurol 12: 947-956.

48. Cooper KH (1968) A means of assessing maximal oxygen intake: correlation between field and treadmill testing. Jama 203: 201-204.

49. Rikli RE, Jones CJ (1998) The reliability and validity of a 6-minute walk test as a measure of physical endurance in older adults. Journal of Aging and Physical Activity 6: 363-375.

50. Harada ND, Chiu V, Stewart AL (1999) Mobility-related function in older adults: assessment with a 6-minute walk test. Arch Phys Med Rehabil 80: 837-841.

51. Steffen TM, Hacker TA, Mollinger L (2002) Age-and gender-related test performance in community-dwelling elderly people: Six-Minute Walk Test, Berg Balance Scale, Timed Up & Go Test, and gait speeds. Phys Ther 82: 128-137.

52. Guyatt GH, Thompson PJ, Berman LB, Sullivan MJ, Townsend M, et al. (1985) How should we measure function in patients with chronic heart and lung disease? J Chronic Dis 38: 517-524.

53. Solway S, Brooks D, Lacasse Y, Thomas S (2001) A qualitative systematic overview of the measurement properties of functional walk tests used in the cardiorespiratory domain. Chest 119: 256-270.

54. Savci S, Inal-Ince D, Arikan H, Guclu-Gunduz A, Cetisli-Korkmaz N, et al. (2005) Six-minute walk distance as a measure of functional exercise capacity in multiple sclerosis. Disabil Rehabil 27: 1365-1371.

55. Matthias S, Nayak US, Isaacs B (1986) Balance in elderly patients: The" get-up and go" test. Arch Phys Med Rehabil 67: 387-389.

56. Podsiadlo D, Richardson S (1991) The timed "Up & Go": a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc39: 142-148.

57. Cattaneo D, Regola A, Meotti M (2006) Validity of six balance disorders scales in persons with multiple sclerosis. Disabil Rehabil 28: 789-795.

58. Morris S, Morris ME, Iansek R (2011) Reliability of measurements obtained with the Timed "Up & Go" test in people with Parkinson disease. Physical Therapy 81: 810-818.

59. Chiu AYY, Au-Yeung SSY, Lo SK (2003) A comparison of four functional tests in discriminating fallers from non-fallers in older people. Disabil Rehabil 25: 45-50.

60. Bohannon RW (1995) Sit-to-stand test for measuring performance of lower extremity muscles. Percept Mot Skills 80: 163-166.

61. Zhang F, Ferrucci L, Culham E, Metter EJ, Guralnik J, et al. (2013) Performance on five times sit-to-stand task as a predictor of subsequent falls and disability in older persons. J Aging Health 25: 478-492.

62. Buatois S, Miljkovic D, Manckoundia P, Gueguen R, Miget P, et al. (2008) Five times sit to stand test is a predictor of recurrent falls in healthy community-living subjects aged 65 and older. J Am Geriatr Soc 56: 1575-1577.

63. Wang CY, Yeh CJ, Hu MH (2011) Mobility-related performance tests to predict mobility disability at 2-year follow-up in community-dwelling older adults. Archives of Gerontology and Geriatrics 52: 1-4.

64. Bohannon RW (2011) Test-retest reliability of the five-repetition sit-to-stand test: a systematic review of the literature involving adults. J Strength Cond Res 25: 3205-3207.

65. Duncan RP, Leddy AL, Earhart GM (2011) Five times sit-to-stand test performance in Parkinson's disease. Arch Phys Med Rehabil 92: 1431-1436.

66. Moller AB, Bibby BM, Skjerbæk AG, Jensen E, Sørensen H, et al. (2012) Validity and variability of the 5-repetition sit-to-stand test in patients with multiple sclerosis. Disabil Rehabil 34: 2251-2258.

67. Ware JE, Kosinski M, Dewey JE, Gandek B (1993) SF-36 Health survey: manual and interpretation guide. Quality Metric Inc.

68. Ware JE, Kosinski M, Turner-Bowker DM, Gandek B (2002) How to score version 2 of the SF-12 Health Survey. Lincoln, RI: A Quality Metric Inc.

69. Ware JE, Kosinski M, Keller SD (1996) A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care 34: 220-233.

70. Jenkinson C, Layte R, Jenkinson D, Lawrence K, Petersen S, et al. (1997) A shorter form health survey: can the SF-12 replicate results from the SF-36 in longitudinal studies? J Public Health Med, 19: 179-186.

71. Gandek B, Ware JE, Aaronson NK, Apolone G, Bjorner JB, et al. (1998) Cross-validation of item selection and scoring for the SF-12 Health Survey in nine countries: results from the IQOLA Project. J Clin Epidemiol 51: 1171-1178.

72. Storr LK, Sørensen PS, Ravnborg M (2006) The efficacy of multidisciplinary rehabilitation in stable multiple sclerosis patients. Mult Scler. 12: 235-242.

73. Soh S, Morris ME, McGinley JL (2011) Determinants of health-related quality of life in Parkinson's disease: A systematic review. Parkinsonism Relat Disord 17: 1-9.

74. Cooney G, Dwan K, Mead G (2014) Exercise for depression. Jama 311: 2432-2433.

75. Schrag A, Jahanshahi M, Quinn N (2000) How does Parkinson's disease affect quality of life? A comparison with quality of life in general population. Mov Disord 15: 1112-1118.

76. Van Uem JMT, Marinus J, Canning C, van Lummel R, Dodel R, et al. (2016) Health-related quality of life in patients with Parkinson's disease – a systematic review based on the ICF model. Neurosci Biobehav Rev 61: 26-34.

77. Motl RW, McAuley E, Snook EN, Gliottoni RC (2009) Physical activity and quality of life in multiple sclerosis: Intermediary roles of disability, fatigue, mood, pain, self-efficacy and social support. Psychol Health Med 14: 111-124.

78. Herring MP, Fleming KM, Hayes SP, Motl RW, Coote SB (2017) Moderators of exercise effects on depressive symptoms in multiple sclerosis: A meta-regression. Am J Prev Med 53: 508-518.

79. Frazzitta G, Bertotti G, Riboldazzi G, Turla M, Uccellini D, et al. (2012) Effectiveness of intensive inpatient rehabilitation treatment on disease progression in parkinsonian patients: a randomized controlled trial with 1-year follow-up. Neurorehabil Neural Repair 26: 144-150.

80. Riazi A, Hobart JC, Lamping DL, Fitzpatrick R, Freeman JA, et al. (2003) Using the SF-36 measure to compare the health impact of multiple sclerosis and Parkinson's disease with normal population health profiles. J Neurol Neurosurg Psychiatry 74: 710-714.

81. Nortvedt MW, Riise T, Myhr KM, Nyland HI (2000) Performance of the SF-36, SF-12, and RAND-36 summary scales in a multiple sclerosis population. Med Care 38: 1022-1028.