

Efficacy of multidisciplinary treatment program on long-term outcomes of individuals with Parkinson's disease

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Abstract—We examined the impact of multidisciplinary clinical management of the Parkinson's Disease Research, Education, and Clinical Center program on Parkinson's disease progression. Initial and follow-up scores on the Part III Motor Examination subscale of the Unified Parkinson's Disease Rating Scale (UPDRS) were examined. Overall, 37 (75.5%) of the 49 patients demonstrated stable or improved UPDRS motor scores at 1- to 3-year follow-up; in the 1-year group ($n = 28$), 22 patients (78.6%) improved, while 6 (21.4%) worsened. In the 2-year group ($n = 15$), 10 (66.7%) improved, while 5 (33.3%) worsened. In the 3-year group ($n = 6$), 5 (83.3%) improved, while 1 (16.7%) worsened. Multidisciplinary interventions included neurology (95.9% of patients), physiatry (93.9%), nursing (87.8%), psychology (42.9%), medication changes (59.2% increases, 18.4% decreases), rehabilitation therapies (physical, occupational, speech-language, 67.3%), functional diagnostic testing (18.4%), support group (16.3%), home exercise instruction (85.7%), and disease and wellness education (81.6%). Improved and worsened patients did not significantly differ on the individual program components. Clinical implications and study limitations are discussed.

Key words: disease progression, intervention, levodopa, movement disorder, multidisciplinary team, neurology, outcomes, Parkinson's disease, rehabilitation, Unified Parkinson's Disease Rating Scale.

INTRODUCTION

Parkinson's disease (PD) affects more than one million adults in the United States and is a major cause of progressive disability. The medical management and societal burden of PD have substantial economic impacts. While well-funded and well-coordinated research programs have been studying the pharmacological treatment of PD since

Abbreviations: IRB = institutional review board; PADRECC = Parkinson's Disease Research, Education, and Clinical Center; PD = Parkinson's disease; SD = standard deviation; UPDRS = Unified Parkinson's Disease Rating Scale; VAMC = Department of Veterans Affairs Medical Center; VHA = Veterans Health Administration.

This material was the result of work supported with resources and the use of facilities at the Southeast PADRECC, Hunter Holmes McGuire VAMC, Richmond, Virginia.

The content of this article is solely the responsibility of the authors and does not necessarily represent the official views of the PADRECC.

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DOI: 10.1682/JRRD.2005.03.0054

1989, the significant difficulties associated with PD persist. In response to the growing prevalence of PD and its concomitant financial burden, the Veterans Health Administration (VHA) established the Parkinson's Disease Research, Education, and Clinical Center (PADRECC) program in 2000. PADRECC is an integrated healthcare delivery model that uses a multidisciplinary assessment and management approach to PD. Both the VHA and the civilian sector have successfully implemented multidisciplinary approaches in the management of specific conditions, including amputation [1], age-related conditions [2–3], traumatic brain injury [4–5], diabetes mellitus [6], and stroke [7]. This investigation expands on an earlier study that assessed the impact of PADRECC multidisciplinary care on individuals with PD at 1-year follow-up [8].

PD is a progressive neurological condition marked by tremor, bradykinesia, postural instability with gait disturbance, and often, cognitive deficits. Since 1987, the Parkinson Study Group has performed a series of multicenter, randomized, controlled trials. In these studies, investigators used standardized clinical scales to examine the impact of pharmaceutical interventions on the progression of PD symptoms [9–13]. Pharmaceutical interventions have been aimed at both neuroprotection (i.e., altering disease course) and symptom management. Using these clinical scales, the Parkinson Study Group has demonstrated that patients have positive responses to and improved symptom management with a number of medications, including deprenyl [10,13], lazabemide [12], rasagiline, and most recently, levodopa [9,14]. These studies initially aimed to delay use of levodopa because patients who have been treated with levodopa for a period of time often display adverse motor side effects such as dyskinesias and clinical fluctuations (e.g., “wearing off” and “on-off” phenomena). After 5 years of treatment, 75 percent of levodopa patients no longer show a smooth, stable, and effective response [15–16]. Interestingly, the recently published ELLDOPA (Earlier vs Later L-DOPA) trial, a multicenter investigation on the impact of different dosages of levodopa versus placebo over a 42-week period, suggests that early use of levodopa has a positive clinical impact on the PD course but a negative impact on nigrostriatal dopamine nerve terminals [14]. Of note, only the highest (and most poorly tolerated) dosing of levodopa resulted in an absolute improvement in function (i.e., improvement over initial baseline status). Each investigation used the traditional medical model of a single discipline (i.e., neurology) approach to clinical care.

Members of the Parkinson Study Group and other research groups have published a number of additional interventional studies and post hoc data analyses assessing the impact of pharmacological agents, including dopamine agonists, on the progression of PD [17–26]. In general, these studies used a neurology clinic model of care. Efficacy was determined by improvements in motor and functional status compared with expected annual decline. These investigations demonstrated variable results in both the natural progression of motor and functional decline in PD and the impact of medications. Some of the investigators described absolute improvements in overall patient function rather than merely improvements relative to the expected decline of placebo-treated patients. Others reported overall worsening but relative improvements compared with the placebo control group. The remaining studies did not demonstrate consistent improvements over time. Chan and Holford identified limitations of the simplistic model of disease progression used in many of these studies, specifically the assumption that disease status and time with disease have a linear relationship, and the lack of attention to within- and between-subject variability [27].

In this investigation, the impact on disease progression of active management by a coordinated, multidisciplinary PD program was evaluated over a 3-year period. Multidisciplinary clinical care allows multiple treatment perspectives on the nature and patient impact of PD symptoms. While traditional individual or “undisciplinary” neurology treatment may access available adjuvant therapies (e.g., physiatry, neuropsychology, rehabilitation therapy, support groups, wellness education) through referral, the comprehensive multidisciplinary care model makes this process seamless and transparent. Prompt, coordinated consultation is easily available because the involved disciplines are all located in the same Department of Veterans Affairs Medical Center (VAMC). Additionally, non-compliance with consultations is more easily tracked and rectified. Furthermore, patients and caregivers are able to reach members of the multidisciplinary team by contacting the PADRECC coordinator, thereby reducing the frustrations and difficulties of “falling through the cracks” that more often accompany the traditional treatment model. Earlier research demonstrated favorable multidisciplinary outcomes at 1-year follow-up [8]. Therefore, we hypothesized that individuals who received multidisciplinary management for longer than 1 year would continue to demonstrate limited disease progression.

METHODS

Subjects

We reviewed the medical records of a subset of 49 consecutive patients enrolled in the PADRECC program at the Hunter Holmes McGuire VAMC in Richmond, Virginia, from October 2000 to December 2004. The PADRECC is a six-site program that was established in 2000 to provide multidisciplinary care to veterans with PD and PD-related movement disorders. Clinical care includes a standardized initial assessment and ongoing management by a dedicated, multidisciplinary treatment team composed of neurologists specializing in movement disorders, an experienced neurology nurse, physical medicine and rehabilitation physicians (physiatrists), a psychologist, and a neurosurgeon trained in deep brain stimulation surgery. Individuals who underwent deep brain stimulation surgery were not included in the analysis. Regular follow-up appointments, team discussions, and specialty referrals (e.g., speech-language pathology, physical and occupational therapy, neuro-ophthalmology) are integral to the program. The steps in the PADRECC clinical pathway are illustrated in the **Figure**.

The 49 patients with neurologist-confirmed PD had been or were being treated with levodopa or dopamine agonists (i.e., ropinirole, pramipexole, pergolide, bromocriptine) at initial PADRECC assessment and had received follow-up assessment at least 8 months after this initial assessment. The individuals were divided into three groups based on timing of most recent follow-up: 12 ± 4 months, 24 ± 4 months, and 36 ± 4 months. Demographics (age at initial assessment, sex, race), clinical characteristics (age at onset of PD symptoms, age at PD diagnosis, PD medications), and motor function (as measured by the Part III Motor Examination subscale of the Unified Parkinson's Disease Rating Scale [UPDRS]) were recorded from initial assessment. Medications and motor function were assessed again at follow-up assessment. In all cases, the neurologists attempted to assess the patients during an "on" phase of their PD (i.e., when motor symptoms were reduced); however, patients were not necessarily excluded based on their "on-off" status at the time of UPDRS assessments because of limitations imposed by timing of assessment, clinical scheduling, patient compliance, and variability of medication effect. We only compared differences between initial and most recent follow-

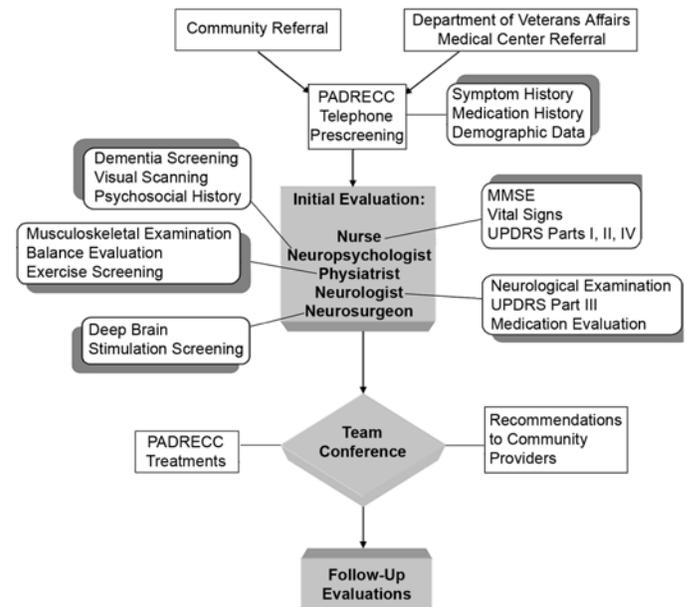


Figure.

Schematic of Parkinson's Disease Research, Education, and Clinical Center (PADRECC) clinical pathway. MMSE = Mini-Mental State Examination, UPDRS = Unified Parkinson's Disease Rating Scale.

up assessments in order to assess the overall efficacy of the program. All applicable institutional review board (IRB) procedures were followed; particular attention was paid to removal of patient identification and preservation of anonymity. Due to the retrospective and post hoc nature of the study, IRB waiver of patient consent was granted.

Measurement Tool: Unified Parkinson's Disease Rating Scale

The UPDRS is the most accepted tool used in clinical research and drug trials for measuring the longitudinal course of PD [28–30]. Only the Part III Motor Examination subscale of the UPDRS was used in this study. The same two fellowship-trained neurologists specializing in movement disorders performed all ratings. The Part III Motor Examination subscale evaluates 27 distinct functions, including speech, tremor (rest and intention), rapid alternating movements, gait, and rigidity. Each function is rated on a scale from 0 to 4, with higher ratings indicating increased impairment. A total of 108 points is possible; 108 represents maximal (or total) disability and 0 represents no disability.

For this investigation, the change in UPDRS score from initial to most recent follow-up assessment was calculated. To demonstrate that the specialized PADRECC

treatment had a value-added benefit, we adopted the criterion of no UPDRS score increase (i.e., did not worsen) as evidence that a patient was a “responder” to the PADRECC program. A patient who had a poorer UPDRS score (i.e., UPDRS change was > 0) at follow-up was considered a “nonresponder.”

Multidisciplinary Interventions

Patients in the PADRECC program received the following multidisciplinary interventions:

1. PD medication management (recommended dosing of levodopa, dopamine agonists, catechol-O-methyltransferase inhibitors, and other symptom-specific agents [e.g., amantadine sulphate]).
2. Neurologist visits.
3. Psychiatrist visits.
4. Neuropsychological evaluation.
5. Nursing visits.
6. Functional diagnostic testing (i.e., gait laboratory, computerized posturography).
7. Rehabilitation therapy (i.e., physical, occupational, kinesitherapy, speech-language).
8. Home exercise program.
9. Support group.
10. Health and wellness education.

The type and number of interventions that each patient received were recorded.

Statistics

Data were analyzed with the Statistical Package for the Social Sciences (SPSS[®]) 13.1 for Windows[®] software program (SPSS, Inc, Chicago, Illinois). Descriptive statistics were analyzed, including the mean \pm standard deviation (SD) and range for the outcome measure (i.e., UPDRS), trend analysis of the UPDRS scores by follow-up assessment, and comparison of the type and number of multidisciplinary interventions received by the patients in the two groups (responders vs nonresponders).

RESULTS

We identified 49 consecutive patients with PD who were being treated with either levodopa or a dopamine agonist at initial assessment and who had returned for at least one follow-up visit 8 or more months after the initial assessment. Of these 49 patients, 28 (57%) had 1 year of

follow-up, 15 (31%) had 2 years of follow-up, and 6 (12%) had 3 years of follow-up. Demographic and clinical characteristics of the patients are shown in **Table 1**.

The patients' changes in UPDRS Part III Motor Examination scores were analyzed. Overall, the entire sample showed a mean improvement in UPDRS score (mean change = -6.2 ± 12.7 SD). Of the 49 patients, 37 (75.5%) demonstrated stable or improved UPDRS scores in the 1- to 3-year follow-up periods (mean change = -1.1 ± 12.1 SD), while the remaining 12 (24.5%) worsened (mean change = 8.7 ± 14.8 SD). In the 1-year follow-up group, 22 patients (78.6%) improved, while 6 (21.4%) worsened. In the 2-year follow-up group, 10 (66.7%) improved, while 5 (33.3%) worsened. Finally, in the 3-year follow-up group, five (83.3%) improved, while only one (16.7%) worsened. Differences for follow-up UPDRS scores and change in UPDRS scores from initial assessment to follow-up for responders and nonresponders are listed in **Table 2**.

The patients received numerous multidisciplinary interventions during the 1 to 3 years of PADRECC follow-up. All patients had at least one neurologist follow-up. Nearly all patients were also seen by the neurology nurse and psychiatrist. More than 60 percent (31, 63.3%) of patients had PD medication changes. Of the 49 patients, 22 (44.9%) had an increase in PD medications during the 3 years of follow-up, 2 (4.1%) had a decrease, 7 (14.3%) had both an increase and a decrease, and 18 (36.7%) had no PD medication changes. No between-group differences for responders and nonresponders were noted for any PD medication adjustments. Patients were most frequently referred for rehabilitation therapy, followed by neuropsychological testing, functional diagnostic testing, and support group. Instruction

Table 1.

Demographic and clinical characteristics of 49 Parkinson's disease (PD) patients receiving multidisciplinary treatment from Parkinson's Disease Research, Education, and Clinical Center program.

Characteristic	<i>n</i>	%
African American	14	29
Caucasian	35	71
	Mean \pm SD	Range
Age (yr)	71.7 \pm 7.7	53–86
Time Since PD Onset (mo)	73.0 \pm 94.2	2–478
Time Since PD Diagnosis (mo)	65.3 \pm 85.2	2–478
Initial UPDRS Part III Motor Examination Score	29.6 \pm 12.5	4–67

SD = standard deviation, UPDRS = Unified Parkinson's Disease Rating Scale.

Table 2.

Age, motor function, medication adjustment, and multidisciplinary interventions for all Parkinson's disease patients studied ($N = 49$) and for two subgroups: responders (patients whose UPDRS scores did not change or worsen from initial to follow-up assessment, $n = 37$) and nonresponders (patients whose UPDRS scores increased [i.e., worsened] from initial to follow-up assessment, $n = 12$).

Measure	All	Responders	Nonresponders	<i>t</i> -Test	<i>p</i> -Value*
Age (yr) [†]	71.2 ± 8.1 (53–86)	70.7 ± 7.7 (54–86)	72.5 ± 9.1 (53–86)	−0.660	0.512
UPDRS Part III Motor Examination Score [‡]					
Initial	29.6 ± 12.5	30.9 ± 12.1	25.0 ± 12.7	−1.451	0.153
Follow-Up	23.2 ± 12.7	19.8 ± 10.0	33.7 ± 14.8	3.681	0.001
Medication Adjustment [‡]					
Increases	59.2 (0.98)	64.9 (1.05)	41.7 (0.75)	−0.904	0.770
Decreases	18.4 (0.20)	13.5 (0.14)	33.3 (0.42)	1.910	0.062
Multidisciplinary Intervention [‡]					
Nurse Visits	87.8 (1.88)	83.8 (1.81)	75.0 (2.08)	0.690	0.494
Neurology Visits	95.9 (3.16)	94.6 (3.16)	75.0 (3.17)	−0.010	0.991
Psychology Evaluations	42.9 (0.43)	45.9 (0.46)	33.3 (0.33)	−0.756	0.453
Physical Medicine and Rehabilitation Visits	93.9 (1.51)	94.6 (1.59)	91.7 (1.25)	−1.364	0.179
Diagnostic Tests	18.4 (0.18)	16.2 (0.16)	25.0 (0.25)	0.672	0.505
Therapy Visits	67.3 (1.24)	67.6 (1.32)	66.7 (1.00)	−0.927	0.359
Support Group	16.3 (0.16)	16.2 (0.16)	16.7 (0.17)	0.036	0.971
Home Exercise	85.7 (0.92)	93.8 (0.92)	91.7 (0.92)	0.014	0.989
Health Education	81.6 (0.82)	86.5 (0.86)	66.7 (0.67)	−1.547	0.129

*Two-tailed test.

[†]Values presented as mean ± standard deviation (range).

[‡]Values presented as % patients (mean adjustment or intervention per patient).

UPDRS = Unified Parkinson's Disease Rating Scale.

on home exercise programs and education on health and wellness were provided to most patients. The responders and nonresponders were not found to differ in the number and types of multidisciplinary interventions received.

DISCUSSION

Recently, investigators have advocated for a more multidisciplinary approach to the care of individuals with PD [31–35]. Two studies from the Royal Surrey County Hospital in the United Kingdom have demonstrated that short-term multidisciplinary services positively affect quality of life and behavioral outcomes [34–35]. The Parkinson's Disease Collaboration, a group of doctors and nurses in the United Kingdom, indicated that development of an integrated care system is the main priority in PD management [33]. Our study is the first multiyear investigation to assess whether a multidisciplinary treatment approach to PD affects neurological outcomes. Importantly, this program demonstrated improved motor function for the vast majority of PD patients. In another recent large long-term (48 months) study assessing the

efficacy of pramipexole versus levodopa in individuals with newly diagnosed PD, half of the subjects (specifically those on levodopa) demonstrated improved UPDRS motor scores [20]. Interestingly, in the present investigation, which examined both medication adjustments and multidisciplinary interventions, three-quarters of the patients maintained and even improved motor function for up to 3 years of follow-up. However, no correlation was identified between medication use or manipulation and improvements in UPDRS motor score. Similarly, the specific impact of any of the 10 PADRECC components on UPDRS motor score could not be demonstrated; however, the overall multidisciplinary approach to clinical care appears to have effectively maintained the patients' motor function. The specific component(s) of the program that positively affected outcome cannot be easily elucidated from these analyses. Clearly, the treatment effect is multifactorial. Replication of these results with stringent, prospective controls is recommended.

Multidisciplinary PD programs have many advantages over the more typical single-clinician approach to PD treatment. Clinicians and support staff dedicated specifically to the management of a single disease set (i.e., movement

disorders) should increase the likelihood of a consistent, structured approach to each patient's care, including standardized assessment and follow-up protocols. Additionally, a multidisciplinary approach should ensure more stringent adherence to established treatment guidelines (e.g., improved screening for dementia, balance and mobility assessment, dosage adjustments), as well as encourage the use of state-of-the-art interventions (e.g., new uses of medications, increased use of exercise protocols). In our experience, the presence of psychologists and psychiatrists is not standard in movement-disorder clinics. The specialized evaluations and treatment recommendations that these clinicians offer may enhance outcomes by, for example, heightening the team members' awareness of depression, anxiety, or family-caregiver burden and increasing their use of nonpharmacological interventions (e.g., exercise, psychotherapy, adaptive equipment). Finally, the intangible elements of enhanced multidisciplinary teamwork, including regular formal and informal clinical discussions and increased attention to ongoing education and specialty training common to multidisciplinary programs, may improve outcomes.

LIMITATIONS

The findings in this investigation are encouraging and suggest that multidisciplinary care positively affects PD outcome. However, given the significant limitations of this study, the results must be considered preliminary. In an outpatient clinical treatment setting in which individuals are managed and monitored over a period of time, control over all potentially confounding variables is exceedingly difficult. Individuals may spontaneously and voluntarily change dietary patterns, exercise levels, sleep habits, and prescription and over-the-counter medications without consulting or informing a clinician. Likewise, living conditions may change, social relationships may vary, and comorbid medical conditions may occur or fluctuate considerably. We assumed that these variables would essentially distribute themselves randomly across patients over time. Thus, no particular reason exists to believe that these factors would produce a pronounced effect on outcome in either direction. Likewise, the pulsatile ("on-off") phenomena of most PD medications was not controlled. Patients' problems correctly quantifying this "on-off" effect (i.e., difficulty specifying whether they are "on" or "off") have been countered by the use of

"on-off" diaries. However, even after 20 to 25 minutes of training [36], patients still had problems differentiating the various motor states. Accordingly, "on-off" diaries were not used in this study. Generally, the belief that our failure to control for this variable pronouncedly affected the study outcome is without basis. Moreover, we assumed that the "on-off" medication effect was randomized; future study of this particular issue may clarify the correctness of this assumption.

PD is a progressive neurological condition with significant clinical variability. The relationship between specific clinical symptoms and disease state or progression has not been established but is unlikely to be linear. While we attempted to determine at each follow-up assessment whether any non-PD morbidity may have contributed to observed changes (typically worsening) in motor status, this cannot always be easily assessed. Similarly, variations in PD symptoms can be greatly affected by timing of medications, although we attempted to optimize the timing of clinical assessments. The complex nature of the VHA clinical delivery system allowed an open-access referral policy, which limited the gathering of all necessary clinical information. Consequently, complete medication histories were not always available. Prior Parkinson Study Group investigations on disease progression may have used individuals with PD who differed from our study cohort (e.g., younger, different disease stage); however, a review of available demographics from these prior studies does not support these differences [10]. While the UPDRS is the "gold standard" for PD assessment, its interrater reliability is limited. Additionally, significant fluctuations in individual patient UPDRS scores may have resulted from the "pulsatile" effects of some PD medications because specific timing of assessments was not always possible. In this study, two neurologists specializing in motor disorders conducted the UPDRS assessments; however, some rating variability may have occurred. Also, the post hoc chart analysis prevented the establishment of a strict schedule for follow-up appointments. Future prospective studies should regulate follow-up intervals more precisely. Finally, while the sample population was robust enough to allow for statistical power, the modest number of subjects and the lack of females may limit the generalizability of these results.

CONCLUSIONS

This investigation represents the first long-range effort to assess the efficacy of a multidisciplinary clinical program in management of PD patients. This study demonstrates that a multidisciplinary approach allows the vast majority of these individuals to maintain or even improve their motor function for up to 3 years after initiation of the program. The specific benefits of the multidisciplinary approach should be further investigated to identify the keys to successful PD management.

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Submitted for publication March 1, 2005. Accepted in revised form June 27, 2005.