Parkinson's Disease—Part 1: Pathophysiology, Symptoms, Burden, Diagnosis, and Assessment

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Abstract

Parkinson's disease (PD) is a chronic neurodegenerative disease associated with substantial morbidity, increased mortality, and high economic burden. Of importance to managed care is that the number of cases of PD are on the rise, paralleling the advancing age of the population, and misdiagnosis is common. Effective management of PD can minimize disability and potentially improve long-term outcomes, which would minimize long-term healthcare costs and medical resource utilization. This article provides a brief review of the epidemiology, pathophysiology, clinical course, and burden of PD.

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Parkinson's disease (PD) is a chronic, progressive, neurodegenerative disease with a multifactorial etiology. Characterized by hallmark signs of bradykinesia, rigidity, tremor, and postural instability, it is superseded only by Alzheimer's disease as the most common neurodegenerative disorder.[1-5] PD exacts a substantial burden on patients, families of patients, and caregivers,[6] and is associated with a significant increase in morbidity and disability; mortality rates are higher and life expectancy lower relative to the general population.[5,7-9] The economic burden of the disease is substantial, related to direct/indirect costs and medical resource utilization.[6,8,10]

Managed care providers and health plans need a broad understanding of PD and its management for 3 principal reasons:

1. The prevalence of PD increases with age.[4,11] This is of growing concern, since the number of cases of PD is increasing as a result of the longer life expectancy in many populations, including the United States, with an increased need for healthcare resources.[2,12]
2. The diagnosis of PD can be easily missed, and misdiagnosis is common.[11,13]
3. Healthcare costs related to PD are projected to rise dramatically in the near future.[10]

This 3-part supplement is being provided to managed care providers to assist them in addressing issues relative to improving the care of patients with PD.

Epidemiology

The prevalence of PD rises from 0.3% in the general US population to 1% to 2% in persons 65 years of age or older; some data indicate a prevalence of 4% to 5% in individuals >85 years.[2,4,5] The usual age of onset is the early 60s, although up to 10% of those affected are 45 years of age or younger; the latter group is referred to as "young-onset" PD.[5,11] In the United States, there are currently up to 1 million with diagnosed PD, which is greater than the combined number of cases of multiple sclerosis, amyotrophic lateral sclerosis (ALS), and muscular dystrophy.[1] About 40,000 cases of PD are diagnosed annually, which by definition does not include the thousands of new cases

that remain undetected.[1] The lifetime risk of PD in males is 2.0% and 1.3% for women.[8] Incidence of the disease appears to be lower in African Americans than Caucasians.[5]

Etiology and Risk Factors

Parkinsonian symptoms can arise from either the neuropathologic condition of PD (idiopathic PD [iPD]) or other forms of parkinsonism.

For neuropathologic PD, about 90% of cases are sporadic, with no clear etiology; an additional 10% have a genetic origin, and at least 11 different linkages with 6 gene mutations have been identified.[11,14,15] Genetic forms of PD are seen more frequently in young-onset PD.[5] A combination of environmental factors or toxins, genetic susceptibility, and the aging process may account for many sporadic cases.[11,14,16]

Secondary forms of parkinsonism can be caused by medications, the sequelae of central nervous system infection, toxins, or vascular/metabolic disorders. Certain neurodegenerative conditions may also exhibit parkinsonian features; these are labeled parkinson-plus or atypical parkinsonian syndromes, and include progressive supranuclear palsy.[5,11,13]

The only proven risk factor for PD is advancing age.[5] Other environmental or lifestyle risk factors associated with development of PD are rural living, exposure to pesticides and herbicides, well-water drinking, and working with solvents.[5,11] However, none of these factors unequivocally has been demonstrated to cause iPD.[5]

Pathophysiology of PD

The pathologic hallmark of PD is degeneration of dopaminergic neurons in the substantia nigra pars compacta (SNc), resulting in depletion of striatal dopamine.[2,15] This neurotransmitter regulates excitatory and inhibitory outflow of the basal ganglia.[2,5,15]

Some surviving neurons contain eosinophilic intracytoplasmic inclusions, or Lewy bodies, which are in part composed of numerous proteins. Protein accumulation is speculated by some to play a prominent role in the pathogenesis of both familial and sporadic PD,[2,14-16] and the appearance of proteins in Lewy bodies tends to support this notion. Lewy bodies appear to represent the aftermath of underlying pathology. Evidence suggests these intracytoplasmic inclusions do not appear deleterious to cells, and may even be cytoprotective.[2] Neurodegeneration of the SNc can occur in the absence of Lewy bodies in both sporadic and familial cases of PD; conversely, Lewy bodies can be present in the absence of neurodegeneration.[2] However, the presence of Lewy bodies is required for pathologic confirmation of a clinical diagnosis of iPD.[5]

The neurodegenerative process in PD is not limited to the SNc, and neuronal loss with Lewy body formation also occurs in other brain regions,[5,15-17] which may account for both motor and nonmotor features of the disease.

Clinical Expression and Course

Four cardinal motor manifestations are the central features of PD: (1) resting tremor, (2) bradykinesia (slowness of movement), (3) rigidity often with a cogwheel quality, and (4) postural instability (impairment of postural reflexes), which occurs later in the disease.[5,18] Symptoms reported by patients when the dominant hand is involved include micrographia (abnormally small, cramped handwriting) and impairment in other fine tasks, such as fastening buttons. Motor symptoms usually begin asymmetrically but gradually spread to the contralateral side,[5,11] although the side of initial involvement tends to remain the most severely affected throughout the course of the disease. Characteristics of these cardinal motor features are shown in **Table 1**.[4,5,11,13] Although these features may also be present in other forms of parkinsonism, asymmetric onset, gradual progression, and response to levodopa in the absence of neurologic findings other than parkinsonism are clues that the patient has iPD.

Clinical presentation may vary from patient to patient, and it is not uncommon for PD symptoms to go unrecognized or unreported for years.[18] A common initial symptom is asymmetric rest tremor (70%-90% of patients).[5,11] This usually involves the thumb or wrist.[4,5,13] A "pill-rolling" motion of the forefinger and thumb at a frequency of 3 to 6 cycles/second is the classical presentation. Tremor is more likely to be the presenting symptom in younger patients, whereas older patients may have more prominent bradykinesia. Tremor may be the most visible sign of PD, but it rarely is the major cause of disability.[5]

Bradykinesia is the most disabling feature of the

Table 1. Motor Features of PD

Resting tremor	70%-90% of patients More commonly distal, involving the hands May be observed as patients rest hands in lap; often "pill-rolling" in nature May have postural component Slow vertical jaw or tongue tremor may be evident, or leg tremor at rest
Bradykinesia	80%-90% of patients Slowness in movement Most disabling symptom of PD May have difficulty turning over in bed or arising from a chair Extreme manifestation is akinesia
Rigidity	>90% of patients Resistance to the passive movement occurring in both flexor and extensor muscles throughout entire range of motion May be "cogwheel" (resistance fluctuates in intensity while limb is passively moved) or "lead-pipe" (continuously rigid) Must distinguish from spasticity, which only has increased flexor tone
Postural instability	Last symptom to appear and reflects progression to advanced stages of PD Predisposes to falls and injuries Early onset is atypical for PD and suggests other cause of parkinsonism Poor or no response to dopaminergic therapy

PD indicates Parkinson's disease.
Adapted from references 4, 5, 11, 13.

disease; it contributes to the inability to arise from a chair or difficulties getting in and out of a car.[11] The extreme of bradykinesia is akinesia, or the inability to initiate movement.[5] Bradykinesia, particularly when combined with rigidity, may manifest as micrographia if the dominant hand is involved. Bradykinesia also presents as very slow movement, hypophonia (weak voice or whispering as a result of un-coordination of muscles of vocalization), reduced dexterity, a masked face and drooling, decreased blink rate, and a slow, shuffling gait.[5,11]

The "cogwheel pattern" of rigidity (fluctuating intensity of resistance while limb is passively moved) is often best detected in the distal part of the limbs, mainly the wrist joint.[5]

Postural instability is a sign of more advanced PD, and one of the most disabling motor features. Postural instability and falls, although initially responsive to treatment, often become treatment resistant. If prominent postural instability occurs early in the disease, the diagnosis of iPD should be questioned.[5,11]

Nonmotor Features. The clinical course of PD is not limited to motor symptoms. A variety of nonmotor symptoms and disorders (Table 2) are common and significantly affect health-related quality of life (HRQOL) of both patient and caregiver.[3,5,9,11,13,19,20] Surveys in PD patients have revealed that close to 90% have at least 1 nonmotor symptom, with about 10% exhibiting 5 nonmotor symptoms.[3]

Increasingly, it is recognized that nonmotor symptoms, especially depression, dementia, and psychosis, contribute to excess disability in PD.[3,9,21] Nonmotor symptoms dominate the clinical picture as PD progresses and may also contribute to shortened life expectancy.[7,9] Most do not respond to, and may be exacerbated by, dopamine replacement therapy.[9] Of concern is that, in contrast to motor symptoms, nonmotor symptoms of PD are frequently unrecognized and either untreated or poorly treated in clinical practice, ultimately leading to increased healthcare costs and utilization.[9]

Depression is frequent in PD and the most common neuropsychiatric disorder, affecting up to 50% of patients.[5,9,19-21] Depression is often comorbid with anxiety and can occur at any stage of the illness, including prior to onset of motor symptoms. Other nonmotor features that may occur early in PD are autonomic dysfunction, cognitive impairment, and olfactory dysfunction (hyposmia, a reduced ability to smell odors, or anosmia, which is loss of smell).

Cognitive impairment in PD is characterized by deficits in executive abilities, memory retrieval deficits, and impairments in attention and visuospatial abilities, with advancing age being the primary risk factor.[5,19] During long-term follow-up of PD patients, a substantial proportion will eventually develop dementia; a prevalence of 78% was reported in a recent long-term prospective study.[20] Dementia is rare in early iPD, and its early occurrence should call into question the diagnosis of PD and may suggest a diagnosis of dementia with Lewy bodies (DLB).[5,13] Anosmia and hyposmia are so common in PD that smell-testing is undergoing evaluation as an early biomarker to identify patients at risk of developing PD; loss of

Table 2. Common Nonmotor Features of PD

Category	Nonmotor Features (Incidence)	Comments
Neuropsychiatric	Depression (up to 50%) Anxiety, including panic attacks Cognitive dysfunction in a range of cognitive domains (50% of patients without dementia) Dementia (20%-80%) Psychosis (<10% of untreated patients; 15%-40% receiving PD medications) Confusion or delirium Apathy	Neuropsychiatric symptoms may cause as much (or more) disability as motor symptoms Depression (commonly coexisting with anxiety) can occur at any time in disease course, including before onset of motor symptoms Cognitive impairment may also be seen early, whereas dementia and psychotic features generally occur in later stages Dementia incidence rises after age 75
ICDs	Obsessional behavior Pathologic gambling Hypersexuality Compulsive shopping Binge eating Other repetitive behaviors	ICDs may be more common in PD than in the general population A neuropsychiatric complication but singled out because of its recent recognition in the literature Etiology unclear; dopamine-agonist therapy, premorbid personality, and younger age have been implicated
Sleep disorders	Insomnia Daytime somnolence (50%) Restless legs and periodic limb movements Sleep apnea Rapid-eye movement behavior disorder (30%) Vivid dreams Sleep-disordered breathing Sudden-onset sleep	Collective prevalence of sleep disorders is estimated between 60% and 90% at some time over the course of the disease May be caused by the underlying neuropathology of PD, the effect of anti-parkinson medications, or associated conditions, such as depression
Autonomic dysfunction	Dysphagia and choking Hypersalivation Impaired gastrointestinal motility Bladder disturbances, such as nocturia, frequency Diaphoresis Orthostatic hypotension Sexual dysfunction Xerostomia Constipation	Autonomic symptoms can occur early on and are relatively common Etiology in part related to degeneration and dysfunction of nuclei regulating autonomic functions, such as dorsal vagal nucleus Constipation may be a risk factor for development of PD
Sensory	Olfactory dysfunction (70%-100%) Pain (common) Paresthesias	Olfactory dysfunction is seen early on and may be a preclinical marker of motor symptoms; no improvement with dopaminergic therapy Pain may be due to motor symptoms, early morning dystonia, or musculoskeletal pain; responds to dopaminergic therapy
Other	Fatigue (common) Diplopia, blurred vision Weight loss Seborrhea	

PD indicates Parkinson's disease; ICDs, impulse control disorders.
Adapted from references 3, 5, 9, 11, 13, 19, 20.

smell is also a sign that has usefulness in differential diagnosis, helping to distinguish PD from other conditions.[5,9] Anosmia does not respond to dopaminergic therapy.[5]

Psychosis, specifically hallucinations and delusional thinking, is also common in PD, seen in 15% to 40% of treated patients[20] and tending to occur later in the disease course. Although there is a clear association between dopaminergic therapy and psychosis, the etiology of psychosis is complex.[20] Other reported risk factors for psychosis include older age, cognitive impairment, visual impairment, sleep disturbances, comorbid depression, and longer duration and increasing severity of PD.[19,20]

Impulse control disorders (ICDs) (Table 2) are increasingly recognized as a relatively common psychiatric disorder in PD, occurring in up to 10% of patients at any given time. The most commonly reported ICDs in PD are compulsive gambling, buying, sexual behavior, and eating, and their occurrence can be devastating to patients and caregivers. Recent research suggests an association between dopamine agonist use and ICDs in PD.

Other Comorbidity. Nonmotor features are considered comorbidities in PD. However, other more general types of comorbidity have been reported separately in various studies. Some of these nonmotor comorbidities include, but are not limited to, falls and injuries (most notably head trauma and hip fracture); cancer, including malignant melanoma; hypertension, stroke, heart failure, and other cardiovascular disease or disorders; impaired glucose tolerance and diabetes; and pneumonia.[22-27] Specific evaluation of these comorbidities is beyond the scope of this review. However, it should be noted that a definite association between these complications and PD remains unclear.

Progression and Mortality. PD is a chronic and slowly progressive disease. Both motor and nonmotor symptoms worsen over time. Prior to the availability of effective symptomatic treatment, the progression of motor symptoms led to severe disability after <10 years of disease.[7] Although dopaminergic therapy effectively treats symptoms, whether the long-term outcome is altered has not been established.[7]

PD is not considered a "fatal" disease,[1] but mortality in patients with PD selected from the community is generally higher than that of the general population, regardless of levodopa or other therapy.[9,28,29] Death is typically caused by secondary complications of the disease; pneumonia is the most common, followed by cardiovascular events (including stroke) and cancer.[9,28]

Life expectancy in PD mirrors its association with increased mortality. Estimates for life expectancy (LE) and age at time of death (AAD) were calculated based on literature review and comparison with the general United Kingdom population.[29] LE and AAD were shown to be reduced for all ages of onset and was greatest in young-onset PD. For the younger cases with onset of PD between 25 and 39 years of age, LE and AAD were 38 years and 71 years, respectively—each about 10 years shorter than for the general population.

In the Sydney trial,[28] mean disease duration from diagnosis until time of death was 9.1 years.

Burden of PD

Patients. For the patient with PD, limitations in functional ability and nonmotor symptoms severely impact HRQOL, and HRQOL deteriorates as the disease progresses.[1,6,9,30,31] In a large study of US veterans, HRQOL was shown to be worse in PD than in 8 other chronic conditions, including stroke, heart disease, and diabetes.[31]

HRQOL is the primary concern of PD patients and their families.[30] Yet HRQOL issues are frequently overlooked by the clinician after diagnosis, largely because of time constraints and the focus on treatment of clinical symptoms; patients and their families also rarely discuss HRQOL aspects of PD with the physician.[30] Inattentiveness to HRQOL and psychosocial issues by the clinician and medical team can adversely affect adherence to treatment, symptom management, and course of the disease.[30]

As there is no cure for iPD, the most important goals of management are to preserve functionality and HRQOL.[4,11,31]

Factors That Impact HRQOL in PD. HRQOL is worse in young-onset versus older-onset patients.[6] Motor fluctuations and dyskinesias secondary to levodopa therapy may also add to HRQOL decline.[6,32] However, the most detrimental impact arises from

neuropsychiatric nonmotor symptoms, especially depression and cognitive dysfunction.[20,21,33] Inability of the patient to overcome depression and cognitive impairment may contribute equally or more so to the impairment seen in activity of daily living (ADL) (eg, Schwab and England scale scores) than limitations imposed by motor impairment.[20,21]

Caregivers. Caregivers of patients with PD also experience poor HRQOL.[6,20,30,34,35] This has been largely overlooked in the overall management of PD. The shift in lifestyle to a caregiver role can be physically and mentally exhausting, leading to enormous stress, fatigue, anxiety, and ultimately depression; social activities of the caregiver are impaired and a financial burden often occurs.[30,34,35] Unlike Alzheimer's disease, where physical disability is not a factor until later in the disease, a double impact on caregiver HRQOL is operative in PD; care is needed for physical limitations of the patient as well as the inevitable cognitive and psychiatric complications, which can begin early in the disease. In addition, caregiver burden has been shown to increase in direct proportion to disease progression and severity.[34,35]

Society. PD is associated with an enormous economic burden in the United States[1,8,10,36] and other countries.[37-41] Estimates of annual directs costs of care in the United States have varied considerably in available studies, from less than $2000 to more than $15,000 per patient. Cost burden is particularly evident in more advanced PD with more severe symptoms, where poorer HRQOL, reduced productivity, and even greater need for healthcare services drive up both direct and indirect costs.[6] Direct costs for drug therapy increase significantly with clinical progression of symptoms.[6] More effective management of PD, especially development of drugs that can slow disease progression, could potentially reduce healthcare resource utilization and associated costs.[6]

In one recent and well-conducted US study, which assessed healthcare utilization and cost data from Medstat's Marketscan Research Databases, Huse et al[10] determined that annual utilization of healthcare services and costs for PD were significantly higher than those in a control group without PD. In particular, compared with controls, patients with PD spent 2 more days in the hospital, 43 more days in long-term care facilities, and received >20 more prescriptions each year. This was reflected in the total annual direct costs per patient with PD, which were about twice as high as controls ($23,101 vs $11,247). The incremental annual direct cost of PD (regression-adjusted estimate) compared with controls was $10,349 per patient. Neuropsychiatric complications, autonomic dysfunction, falls, and injuries in the PD group accounted for a significant proportion of direct costs. Based on indirect costs of $25,326 per year obtained from previous estimates, the total economic burden of PD in the United States was projected to be $23 billion annually. Of this total burden, almost 70% was related to indirect costs in terms of productivity loss and provision of uncompensated care by family and household members. Inpatient care (including nursing homes) and outpatient care accounted for 20% and 8% of the total, respectively. Prescription drug costs were responsible for about 4%.

Diagnosis of PD

Stepwise Approach. The diagnosis of PD remains a clinical one. The following 3-step approach is suggested, which is adapted from criteria established by the UK Parkinson's Disease Society Brain Bank,[5,42] as well as other published diagnostic criteria.

Step 1. Identification of a Parkinsonian Syndrome. Commonly used criteria are the presence of bradykinesia and at least 1 of the following: muscular rigidity, 4- to 6-Hz resting tremor, and/or postural instability.[5,42]

Step 2. Exclusion of Other Causes of Parkinsonism. Differentiation of PD from other causes of parkinsonism is paramount. This includes separation from secondary (symptomatic) forms and atypical (parkinson-plus) syndromes, which can often be challenging.

SECONDARY OR SYMPTOMATIC forms include drug-induced parkinsonism, most commonly related to antipsychotics and antiemetic agents; postinfectious parkinsonism (eg, sequelae of West Nile viral encephalitis); structural lesions, such as stroke or hydrocephalus; vascular lesions; metabolic conditions, including Wilson's disease; trauma (post-

traumatic parkinsonism); and toxic insults, such as those caused by carbon monoxide, manganese, or 1-methyl-4-phenyl 1,2,3,6-tetrahydropyridine (MPTP).[4,5,11,13,43] Prescribed medications frequently implicated in the development of parkinsonism are haloperidol, risperidone, metoclopramide, and prochlorperazine.[13]

ATYPICAL (PARKINSON-PLUS) CONDITIONS include Alzheimer's disease with extrapyramidal signs; progressive supranuclear palsy; multiple system atrophy, such as Shy-Drager syndrome; corticobasal ganglionic degeneration; DLB; spinal cerebellar ataxias; striatonigral degeneration; and ALS/parkinsonism-dementia complex of Guam.[4,5,11,13]

Step 3. Identification of Supportive Features. Several supportive criteria can increase the positive predictive value of the clinical diagnosis of PD against the gold standard of pathology confirmation.[5,42] At least 3 supportive features add greatly to diagnostic confidence. Important is a response to an adequate challenge of levodopa, which is required for clinical diagnosis of PD.[4,5] Olfactory dysfunction may be highly useful in distinguishing PD from other types of parkinsonism.[4]

Use of Neuroimaging. Neuroimaging does not play a role in diagnosing PD. Computed tomography and magnetic resonance imaging (MRI) show no specific patterns related to PD[4,5] and are not indicated in the patient with typical features of the disease. However, neuroimaging may be useful in patients presenting with atypical features to help rule out other causes of parkinsonism. Some specialists recommend MRI: (1) for patients who present atypically; (2) for patients responding suboptimally to therapy; or (3) if there is concern about alternative etiologies of parkinsonian symptoms.[5]

Patient Assessment

The standard and most commonly used method of assessing motor symptoms and clinical status over time in PD is the Unified Parkinson's Disease Rating Scale (UPDRS). It has proved effective for patient management and clinical research.[9] Other methods that have proven useful for clinical assessment are the modified Hoehn and Yahr staging scale and the Schwab and England ADL scale.[6,44]

The UPDRS consists of 4 parts that assess mental and behavior problems, ADLs, motor symptoms, and complications of therapy.[44,45] However, this scale has shortcomings. Some questions and responses lack clarity; nonmotor symptoms are not adequately addressed (especially neuropsychiatric); patient self-perceptions are limited; and there are weaknesses in motor assessments.[9,46,47] Overall, the UPDRS does not completely capture the breadth of the disease. In particular, recognition of the important contribution of nonmotor symptoms to disability is not reflected in the questions.

In 2001, the Movement Disorder Society (MDS) sponsored a critique of the UPDRS, which led to its revision.[46] The new scale—the MDS-Sponsored UPDRS Revision (MDS-UPDRS)—contains more questions than the original scale, but time to complete is similar. The new design purportedly permits greater detection of small changes and mild disabilities, and has new nonmotor-symptom entries. Some new additions include other nonmotor symptoms, such as anxiety, fatigue, constipation, and urinary problems, and additional motor assessments, including toe-tapping. Patient input is increased with questions regarding activities/experiences (eg, hobbies, feeding, cooking).

The MDS-UPDRS will be available for routine use sometime in 2008.

Nonmotor Symptoms and HRQOL. Although the MDS-UPDRS represents an improvement for assessing nonmotor symptoms, a nonmotor scale focusing only on this symptom complex would be a welcome addition to the clinician. Such scales are not yet available, but 2 are currently under development: the PD Nonmotor Symptom Questionnaire (NMSQuest) and a PD nonmotor symptom scale.[9] Each offers a more comprehensive assessment of nonmotor symptoms and may appear as appendices to the UPDRS after validation.[9] NMSQuest is specifically designed to assist the busy clinician in identifying nonmotor symptoms early.[9] The Scales for Outcomes in Parkinson's Disease (SCOPA) are currently available to assess nonmotor (and motor) symptoms, but only for a specific outcome, such as autonomic symptoms or sleep.

Instruments to measure patient HRQOL provide more specific information on health burden and

total disease impact, and can be used to supplement clinical scales.[6] One of the most commonly used is the Parkinson's Disease Questionnaire-39 (PDQ-39), which is an 8-dimension, disease-specific instrument. It has good internal consistency, retest reliability, construct validity, and sensitivity; it is able to discriminate between levels of severity and is sensitive to changes that matter to the patient but are not the main focus of the clinician.[6] Although considered the tool of choice,[6] some clinicians have found that the HRQOL utility of PDQ-39 is confounded by motor and nonmotor assessments.

Other HRQOL instruments specific to PD and that may be useful are the Parkinson's Impact Scale and Parkinson's Disease Quality of Life Scale.[6]

Conclusion

The number of cases of PD will increase dramatically in the future, accompanied by a rise in medical resource utilization and healthcare costs. Studies have shown difficulties in diagnosing PD and poor recognition of its disabling nonmotor symptoms, suggesting the need to enhance awareness of techniques for both diagnosing and monitoring this disease. More and more patients with PD will be seen by the clinician in years to come, and accurate diagnosis increases the chance of effective treatment and reduced disability over time, which reduces direct and indirect healthcare costs. The comorbid neuropsychiatric nonmotor symptoms of PD, such as depression and cognitive impairment, are particularly important, because they may be more disabling to the patient than motor symptoms. Screening for neuropsychiatric symptoms, and their effective treatment and monitoring, will improve the functioning and HRQOL of the patient with PD, which are primary goals of management.

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