The aim of the Canadian Guidelines on Parkinson’s Disease is to enhance the care for all Canadians with Parkinson’s Disease that:
• is based on the best published evidence
• involves expert consensus when there is a lack of evidence
• offers practical clinical advice
• takes into account patient choice and informed decision making
• is relevant to the Canadian Health Care System

These recommendations are intended to serve as a guide for health care providers, and clinical discretion should be used by all who are following the Canadian Parkinson’s Guideline recommendations. The definitive judgment is made by the appropriate healthcare professional(s) based on all the data available for an individual person. It is recognized that resource problems may make it difficult to put into practice every recommendation in these guidelines. However, they are meant to improve the standard of care and access to care for individuals with Parkinson’s in all regions of Canada. Guidelines are not meant to be a substitute for expert evaluation and management and that wherever possible, referral to a specialized, multidisciplinary clinic is still recommended. The full guidelines, including details of the development process, are available at www.parkinsonclinicalguidelines.ca. The original source and evidence grade are referenced at the end of each Canadian recommendation (see Table 1).

Section 1
Communication

A person-centred approach to care and treatment should be cultivated for people living with Parkinson’s disease (PD). It relies upon open communication with health care professionals who are then able to provide quality care. People with Parkinson’s should have the opportunity to make informed decisions based on full disclosure of all relevant information. Care decisions should be based upon best available evidence and provided by applicable professional standards.

Issues to consider when communicating with people with Parkinson’s and their caregivers:
• Style, manner and frequency of communication that is compassionate and respectful
• Ease of access for those receiving information in a timely and appropriate manner throughout the progression of Parkinson’s
• Honesty and sensitivity in tailoring information to meet changing medical needs
• Encouragement of self-management by people with Parkinson’s to meet individual needs and preferences
• Inclusion of caregivers who are also impacted by Parkinson’s and require information and support

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Established as effective, ineffective, or harmful for the given condition in the specified population.</td>
</tr>
<tr>
<td>B</td>
<td>Probably effective, ineffective, or harmful for the given condition in the specified population.</td>
</tr>
<tr>
<td>C</td>
<td>Possibly effective, ineffective, or harmful for the given condition in the specified population.</td>
</tr>
<tr>
<td>D</td>
<td>Expert opinion, formal consensus.</td>
</tr>
<tr>
<td>U</td>
<td>Data inadequate or conflicting given current knowledge, treatment is unproven.</td>
</tr>
<tr>
<td>GPP</td>
<td>Good practice point.</td>
</tr>
</tbody>
</table>

Table 1: Simplified Grading scheme from NICE, EFNS and AAN Guidelines

AAN: American Academy of Neurology; NICE: National Institute for Health and Clinical Excellence; EFNS: European Federation of Neurological Societies

C1 Communication with people with PD should be aimed towards empowering them to participate in the judgments and choices about their own care. NICE Level D

C2 Discussions should be aimed at achieving a balance between the provision of honest, realistic information about the condition and the promotion of a feeling of optimism. NICE Level D

C3 Because people with PD may develop impaired cognitive ability, a communication deficit and/or depression, they should be provided with: both oral and written communication throughout the course of the disease, which should be individually tailored and reinforced as necessary; and consistent communication from the professionals involved. NICE Level D (GPP)

C4 Families and caregivers should be given information about the condition, their entitlements to care assessment and the support services available. NICE Level D (GPP)
C5 People with PD should have a comprehensive care plan agreed between the individual, their family and/or caregivers and all healthcare providers. NICE Level D (GPP)

C6 People with PD should be offered an accessible point of contact with specialist services. NICE Level D (GPP)

C7 Palliative care requirements of people with PD should be considered throughout all phases of the disease. NICE Level D (GPP)

C8 People with PD and their caregivers should be given the opportunity to discuss end-of-life issues with appropriate healthcare professionals. NICE Level D (GPP)

Section 2

Diagnosis and Progression

Parkinson’s disease is a complex disorder that can be difficult to diagnose clinically, especially in the early stages. Diagnosis based on etiology is impractical because no single cause of PD has been identified. Currently the diagnosis of PD is based predominantly on the clinical features.

C9 PD should be suspected in people presenting with tremor, stiffness, slowness, balance problems and/or gait disorders. NICE Level D (GPP)

There is no ideal way to define PD and distinguish it from other parkinsonian syndromes. Nevertheless, PD needs to be differentiated from other forms of parkinsonism, and should also be distinguished from secondary causes such as drugs, neurotoxins, and structural brain lesions as well as other causes of tremor.

C10 Determining the presence of the following clinical features in early stages of disease should be considered to distinguish PD from other parkinsonian syndromes:
- Falls at presentation and early in the disease course
- Poor response to levodopa
- Symmetry at onset
- Rapid progression (to Hoehn and Yahr stage 3 in three years)
- Lack of tremor
- Dysautonomia (urinary urgency/incontinence and fecal incontinence, urinary retention requiring catheterization, persistent erectile failure or symptomatic orthostatic hypotension). AAN Level B

C11 People with suspected PD should be referred quickly* and untreated to a specialist with expertise in the differential diagnosis of this condition. NICE Level B

(*should be seen within 6 weeks, but new referrals in later disease with more complex problems require an appointment in 2 weeks)

Parkinson’s disease involves the degeneration of midbrain dopamine neurons, along with other catecholamine neurons, and the presence of Lewy bodies. About 20% of patients diagnosed with early stage PD have an alternative diagnosis at autopsy. Given the potential error in making a diagnosis of PD, patients should be followed closely and the diagnosis reconsidered if atypical features emerge.

C12 Clinicians should be encouraged to discuss with patients the possibility of tissue donation to a brain bank for purposes of diagnostic confirmation and research. NICE Level D (GPP)

Several drug challenges or diagnostic tests have been proposed to aid in the diagnosis of PD and/or in the differentiation between PD and other parkinsonian syndromes. However, to date, no single test has been shown to have sufficient sensitivity and specificity to reliably diagnose PD or distinguish PD from other forms of parkinsonism.

C13 There is insufficient evidence to determine whether levodopa challenge or olfaction testing have any advantage over the clinical diagnostic criteria of PD. AAN Level U

C14 The following may not be useful in differentiating PD from other parkinsonian syndromes: GH stimulation with clonidine, electrooculography, and SPECT scanning. AAN Level C

C15 There is insufficient evidence to support or refute the following as a means of distinguishing PD from other parkinsonian syndromes: urodynamics, autonomic testing, urethral or anal EMG, MRI, brain parenchyma sonography, and FDG PET. AAN Level U

Parkinson’s disease is a heterogeneous disorder with clinical presentation varying substantially from patient to patient. A number of studies have examined the clinical PD subtype, the associated co-morbidities as well as response to treatment that were correlated with a more rapid progression of PD.

C16 In patients with newly diagnosed PD, older age at onset and rigidity/hypokinesia as an initial symptom should be used to predict more rapid rate of motor progression. AAN Level B

C17 The presence of associated comorbidities (stroke, auditory deficits, and visual impairments), Postural Instability/Gait difficulty (PIGD), and male sex may be used to predict faster rate of motor progression. AAN Level C

C18 Tremor as a presenting symptom may be used to predict a more benign course and longer therapeutic benefit to levodopa. AAN Level C

C19 Older age at onset and initial hypokinesia/rigidity should be used to predict earlier development of cognitive decline and dementia. AAN Level B

C20 Older age of onset, dementia, and decreased dopamine responsiveness may be used to predict earlier nursing home placement as well as decreased survival. AAN Level C

Clinical trials of putative neuroprotective compounds have been explored and, although some compounds show promise, results in general have been unrewarding, in part because of the challenges associated with establishing neuroprotection for compounds that may also have a symptomatic effect.
C21 Vitamin E should not be used as a neuroprotective therapy for people with PD. NICE Level A

C22 Co-enzyme Q10, dopamine agonists, monoamine oxidase B (MAO-B) inhibitors should not be used as a neuroprotective therapy for people with PD, except in the context of clinical trials. NICE Level B

C23 There is insufficient evidence to support or refute the use of amantadine or thalamotomy for neuroprotection. AAN Level U

C24 There is no long term evidence to recommend levodopa for neuroprotection. AAN Level U

Section 3

General Treatment Considerations

There are a wide number of symptomatic treatments that are available for PD. These include medications, surgical procedures, physiotherapy, occupational therapy and other support services. All of these treatments can have a significant impact on improving an affected individual’s quality of life and should be available. A balance between the side effects of the medication and the benefit often becomes more difficult with time. Medication schedules become more complex and the timing of when medications are given becomes crucial.

C25 Anti-parkinsonian medication should not be withdrawn abruptly or allowed to fail suddenly due to poor absorption (for example, gastroenteritis, abdominal surgery) to avoid the potential for acute akinesia or neuroleptic malignant syndrome. NICE Level D (GPP)

C26 The practice of withdrawing patients from their anti-parkinsonian drugs (so-called ‘drug holidays’) to reduce motor complications should not be undertaken because of the risk of neuroleptic malignant syndrome. NICE Level D (GPP)

C27 In view of the risks of sudden changes in anti-parkinsonian medication, people with PD who are admitted to hospital or care homes should have their medication: A) given at the appropriate times, which in some cases may mean allowing self-medication; B) adjusted by, or adjusted only after discussion with, a specialist in the management of PD. NICE Level D (GPP)

C28 Clinicians should be aware of dopamine dysregulation syndrome (impulse control disorders), an uncommon disorder in which dopaminergic medication misuse is associated with abnormal behaviours, including hypersexuality, pathological gambling and stereotypic motor acts. This syndrome may be difficult to manage. NICE Level D (GPP)

Section 3A

Pharmacological therapy for motor symptoms in early PD

The decision about initiation of pharmacologic therapy in PD patients should be tailored to the individual with the goal of reducing motor symptoms, and improving quality of life without causing side effects. There is no one medication which is recommended for treatment initiation. Factors that influence this decision include: symptom severity, whether the symptoms affect the dominant hand, embarrassment, ability to continue working and/or participate in activities or hobbies, cost, and patient preference. If symptoms are very mild, the patient may choose not to begin therapy.

C29 It is not possible to identify a universal first-choice drug therapy for people with early PD. The choice of drug first prescribed should take into account:
- clinical and lifestyle characteristics
- patient preference, after the patient has been informed of the short- and long-term benefits and drawbacks of the drug classes. NICE Level D (GPP)

C30 Levodopa may be used as a symptomatic treatment for people with early PD. NICE Level A

C31 The dose of levodopa should be kept as low as possible to maintain good function in order to reduce the development of motor complications. NICE Level A

C32 Modified-release levodopa preparations should not be used to delay the onset of motor complications in people with early PD. NICE Level A

C33 Dopamine agonists may be used as a symptomatic treatment for people with early PD. NICE Level A

C34 A dopamine agonist should be titrated to a clinically efficacious dose. If side effects prevent this, another agonist or a drug from another class should be used in its place. NICE Level D (GPP)

C35 If an ergot-derived dopamine agonist is used, the patient should have a minimum of renal function tests, erythrocyte sedimentation rate (ESR) and chest radiograph performed before starting treatment, and annually thereafter. NICE Level D (GPP)

C36 In view of the monitoring required with ergot-derived dopamine agonists, a non-ergot-derived agonist should be preferred in most cases. NICE Level D (GPP)

C37 MAO-B inhibitors may be used as a symptomatic treatment for people with early PD. NICE Level A

C38 Amantadine may be used as a treatment for people with early PD but should not be a drug of first choice. NICE Level D (GPP)

C39 Anticholinergics may be used as a symptomatic treatment typically in young people with early PD and severe tremor, but should not be drugs of first choice due to limited efficacy and the propensity to cause neuropsychiatric side effects. NICE Level B
Section 3B
Pharmacological therapy for motor symptoms in later PD

Levodopa is the most effective treatment for PD. In the early stages of disease, the clinical response to levodopa is prolonged; however, within a few years the duration of benefit from each dose may become progressively shorter. This phenomenon is referred to as “end of dose deterioration” or “wearing-off”. Eventually patients may experience more unpredictable fluctuations including: on-off responses and freezing as well as involuntary movements broadly referred to as dyskinesias. These motor disabilities may have a significant impact on quality of life.

C41 It is not possible to identify a universal first-choice adjuvant drug therapy for people with later PD. The choice of adjuvant drug first prescribed should take into account:
- clinical and lifestyle characteristics
- patient preference, after the patient has been informed of the short- and long-term benefits and drawbacks of the drug classes. NICE Level D (GPP)

C42 For patients with PD with motor fluctuations the available evidence suggests: Entacapone and rasagiline should be offered to reduce off time. AAN Level A

C43 Pramipexole and ropinirole should be considered to reduce off time. Pergolide is not available in Canada secondary to its association with valvular fibrosis. AAN Level B

C44 Modified-release levodopa preparations may be used to reduce motor fluctuations in people with later PD but should not be drugs of first choice. NICE Level B

C45 Amantadine may be considered for patients with PD with motor fluctuations in reducing dyskinesias. AAN Level C

Section 3C
Treatment - Surgery

The surgical treatment for PD is currently considered in advanced patients when the optimized medical treatment has failed in treating motor symptoms (such as motor fluctuations and/or dyskinesia). Deep brain stimulation (DBS) is currently the surgical treatment of choice in advanced PD patients. Compared to ablative surgery, DBS can be adjusted over time to address disease progression, has reversible effects, and can be used bilaterally to improve symptoms. The current targets for PD are the ventral intermediate (VIM) thalamic nucleus, the subthalamic nucleus (STN), and the globus pallidus internus (GPI).

C46 DBS of the STN may be considered as a treatment option in PD patients to improve motor function and to reduce motor fluctuations, dyskinesia, and medication usage. Patients need to be counselled regarding the risks and benefits of this procedure. AAN Level C

C47 Bilateral GPI stimulation may be used in people with PD who:
- have motor complications that are refractory to best medical treatment
- are biologically fit with no clinically significant active comorbidity
- are levodopa responsive
- have no clinically significant active mental health problems, for example depression or dementia. NICE Level D

C48 With the current evidence it is not possible to decide if the STN or GPI is the preferred target for DBS for people with PD, or whether one form of surgery is more effective or safer than the other. In considering the type of surgery, account should be taken of:
- clinical and lifestyle characteristics of the person with PD
- patient preference after the patient has been informed of the potential benefits and drawbacks of the different surgical procedures. NICE Level D

C49 Thalamic DBS may be considered as an option in people with PD who predominantly have severe disabling tremor and where STN stimulation cannot be performed. NICE Level D

C50 Preoperative response to levodopa should be considered as a factor predictive of outcome after DBS of the STN. AAN Level B

C51 There is insufficient evidence to make any recommendations about factors predictive of improvement after DBS of the GPI or VIM nucleus of the thalamus in PD patients. AAN Level U

C52 Age and duration of PD may be considered as factors predictive of outcome after DBS of the STN. Younger patients with shorter disease durations may possibly have improvement greater than that of older patients with longer disease durations. AAN Level C

Section 3D
Treatment - Other Treatment Options

Previously, motor function received the primary attention of patients and physicians alike. This naturally led to concentration on pharmacological therapies for PD. More recently, non-motor symptoms have become recognized as a major source of disability in PD and treatment focus has shifted to quality of life and maintaining it in advanced disease.

C53 People with PD should have regular access to the following:
- clinical monitoring and medication adjustment
- a continuing point of contact for support, including home visits, when appropriate
- a reliable source of information about clinical and social matters of concern to people with PD and their caregivers which may be provided by a Parkinson’s disease nurse specialist. NICE Level C
C54 Physical and exercise therapies should be available for people with PD. Particular consideration should be given to:
  • gait re-education, improvement of balance and flexibility
  • enhancement of aerobic capacity
  • improvement of movement initiation
  • improvement of functional independence, including mobility and activities of daily living
  • provision of advice regarding safety in the home environment. NICE Level B

C55 Occupational therapy should be available for people with PD. Particular consideration should be given to:
  • maintenance of work and family roles, home care and leisure activities
  • improvement and maintenance of transfers and mobility
  • improvement of personal self-care activities, such as eating, drinking, washing and dressing
  • environmental issues to improve safety and motor function
  • cognitive assessment and appropriate intervention.
  NICE Level D (GPP)

C56 Speech and language therapy should be available for people with PD. Particular consideration should be given to:
  • improvement of vocal loudness and pitch range, including speech therapy programs such as Lee Silverman Voice Treatment (LSVT) NICE Level B
  • teaching strategies to optimize speech intelligibility
  • ensuring an effective means of communication is maintained throughout the course of the disease, including use of assistive technologies. NICE Level D (GPP)
  • review and management to support safety and efficiency of swallowing and to minimize the risk of aspiration.
  NICE Level D (GPP)

C57 There is insufficient evidence to support or refute the use of acupuncture, manual therapy, biofeedback or the Alexander technique in the treatment of PD. AAN Level U

C58 Clinicians should have a low threshold for diagnosing depression in PD. NICE Level D (GPP)

C59 Clinicians should be aware that there are difficulties in diagnosing mild depression in people with PD because the clinical features of depression overlap with the motor features of PD. NICE Level D (GPP)

C60 The management of depression in people with PD should be tailored to the individual, in particular, to their co-existing therapy. NICE Level D (GPP)

C61 Amitriptyline may be considered in the treatment of depression associated with PD. AAN Level C

Psychotic Symptoms

Psychotic features occur frequently in later stages of PD with a typical progression from illusions of presence, through pseudo hallucinations (preservation of awareness of false nature of the phenomenon) to true hallucinations. Visual hallucinations are the most common although auditory hallucinations also occur. Paranoia is a common accompaniment.

Not all hallucinations require treatment. If they are sufficiently problematic to the patient or caregiver then alteration in treatment is needed.

C62 All people with PD and psychosis should receive a general medical evaluation and treatment for any precipitating condition. NICE Level D (GPP)

C63 Reduce polypharmacy. Reduce/stop anticholinergic antidepressants, reduce/stop anxiolytics/sedatives. EFNS (GPP)

C64 Consideration should be given to gradually withdrawing antiparkinsonian medication that might have triggered psychosis in people with PD. NICE Level D (GPP)

C65 Reduce antiparkinsonian drugs. Stop anticholinergics, stop amantadine, reduce/stop dopamine agonists, reduce/stop MAO-B and COMT inhibitors, lastly, reduce levodopa. Stopping antiparkinsonian drugs can be at the cost of worsening motor symptoms. EFNS (GPP)

C66 Mild psychotic symptoms in people with PD may not need to be actively treated if they are well tolerated by the patient and caregiver. NICE Level D (GPP)

C67 Typical antipsychotic drugs (such as phenothiazines and butyrophenones) should not be used in people with PD because they exacerbate the motor features of the condition. NICE Level D (GPP)

C68 For patients with PD and psychosis, olanzapine should not be routinely considered. AAN Level B

C69 Clozapine may be used in the treatment of psychotic symptoms in PD, but registration with a mandatory monitoring scheme is required. It is recognized that few
specialists caring for people with PD have experience with clozapine. NICE Level B

C70 For patients with PD and psychosis, quetiapine may be considered. AAN Level C

Dementia

Dementia in PD is common, especially in those with an older age of onset and its frequency increases with disease duration. As patients with PD live longer this problem will become an increasingly difficult management problem.

As with psychosis, after ruling out other potential medical disorders contributing to dementia (e.g., thyroid dysfunction, B12 deficiency), it is generally recommended that a simplification of medications be undertaken to minimize potential untoward central nervous system effects that accentuate the cognitive dysfunction.

C71 Discontinue potential aggravators:
• Anticholinergics. EFNS Level B
• Amantadine, tricyclic antidepressants, benzodiazepines, tolterodine and oxybutynin. EFNS Level C

C72 Donepezil should be considered for the treatment of dementia in PD. AAN Level B

C73 Rivastignine should be considered for the treatment of dementia in PD or Dementia with Lewy Bodies. AAN Level B

Section 4B

Sleep disorders

A variety of sleep disorders affect patients with PD. The major sleep disorders in PD include insomnia, excessive daytime somnolence, REM sleep behavior disorder, and restless legs syndrome. Physicians are advised to be aware of their provincial legislation regarding driving in patients who are experiencing sleep attacks.

C74 A full sleep history should be taken from people with PD who report sleep disturbance. NICE Level D (GPP)

C75 Good sleep hygiene should be advised in people with PD with any sleep disturbance and includes:
• avoidance of stimulants (for example, coffee, tea, caffeine) in the evening
• establishment of a regular pattern of sleep
• comfortable bedding and temperature
• provision of assistive devices, such as a bed lever or rails to aid with moving and turning, allowing the person to get more comfortable
• restriction of daytime siestas
• advice about taking regular and appropriate exercise to induce better sleep
• a review of all medication and avoidance of any drugs that may affect sleep or alertness, or may interact with other medication (for example, selegiline, antihistamines, H2 antagonists, antipsychotics and sedatives). NICE Level D (GPP)

C76 Care should be taken to identify and manage restless legs syndrome (RLS) and rapid eye movement (REM) sleep behaviour disorder in people with PD and sleep disturbance. NICE Level D (GPP)

C77 People with PD who have sudden onset of sleep should be advised not to drive and to consider any occupational hazards. Attempts should be made to adjust their medication to reduce its occurrence. NICE Level D (GPP)

C78 Modafinil may be considered for daytime hypersonmolence in people with PD. NICE Level D (GPP)

Section 4C

Autonomic dysfunction. Treatment – General considerations

Autonomic dysfunction encompasses cardiovascular, gastrointestinal, urogenital and thermoregulatory disorders.

Autonomic dysfunctions, especially orthostatic hypotension, nocturia and constipation, have significant impact on quality of life. Despite the frequency and breadth of the symptoms evidence regarding specifics of management is poor. Due to the lack of randomized controlled trials across these symptoms, many of the recommendations are based on data from treating these symptoms in non-parkinsonian individuals.

C79 People with PD should be treated appropriately for the following autonomic disturbances: NICE Level D (GPP)
• urinary dysfunction
• weight loss
• dysphagia
• constipation
• erectile dysfunction
• orthostatic hypotension
• excessive sweating
• sialorrhoea

Urinary Dysfunction

The most common forms of urinary dysfunction are urgency, frequency and nocturia. In men, prostatic hypertrophy must be ruled out. A urological assessment is always warranted if pathology different than PD is suspected.

C80 General measures for treating urinary urgency and incontinence include avoiding coffee before bedtime, limit water ingestion before bedtime, etc.
• Add peripherally acting anticholinergic drugs. EFNS (GPP)

Constipation

Constipation can predate the onset of PD symptoms by decades. However, dysmotility in PD is not only a function of lower gastrointestinal (GI) dysfunction but also due to slowing of transit time through the entire GI tract. Evacuating stool is also an issue in many patients if the stool is hard. Again, good quality data is lacking for most suggested therapies for treating constipation in PD.

Canadian Guidelines on Parkinson’s Disease 6
For gastrointestinal motility problems in PD:

- apply general measures for treating constipation. These include diet, laxatives, etc
- Reduce or discontinue drugs with anticholinergics activity. EFNS (GPP)
- Add domperidone. EFNS Level B

Orthostatic Hypotension

Important causes of orthostatic hypotension include: poor intake of fluids, side-effects of general medications such as antihypertensives, antidepressants, diuretics, other medical conditions such as cardiac dysfunction, diabetic neuropathy, PD dysautonomia, and side-effects of all PD medications especially dopamine agonists. A home blood pressure cuff for monitoring is often useful to document the severity and times of the orthostatic symptoms.

For orthostatic hypotension general measures would include:

- avoid aggravating factors such as large meals, alcohol, exposure to a warm environment and drugs known to cause orthostatic hypotension such as diuretics or antihypertensive drugs. Levodopa and dopamine agonists may also induce orthostatic hypotension
- increase salt intake in symptomatic orthostatic hypotension
- head-up tilt of the bed at night
- wear elastic stockings
- highlight postprandial effects. In some patients, hypotension occurs only postprandially. Warning the patient about this effect and taking frequent small meals may be helpful. EFNS (GPP)

Drug therapy for orthostatic hypotension would include:

- add midodrine EFNS Level A
- add fludrocortisone EFNS (GPP)

Erectile dysfunction

In addition to the dysautonomia caused by the PD, mood dysfunction, motor disability and side effects of medications may also contribute significantly.

For the treatment of erectile dysfunction in PD add sildenafil. EFNS Level A

For a full list of references used to develop the guidelines, see www.parkinsonclinicalguidelines.ca.

Parkinson Society Canada
Société Parkinson Canada

These guidelines are endorsed by the Canadian Neurological Sciences Federation.