National Institute for Health and Clinical Excellence

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Parkinson's disease

Diagnosis and management in primary and secondary care

NICE clinical guideline 35
Developed by the National Collaborating Centre for Chronic Conditions

NICE clinical guideline 35
Parkinson's disease: diagnosis and management in primary and secondary care

Ordering information
You can download the following documents from www.nice.org.uk/CG035

- The NICE guideline (this document) – all the recommendations.
- Information for the public – information for people with Parkinson's disease and their carers.
- The full guideline – all the recommendations, details of how they were developed, and summaries of the evidence on which they were based.

This guidance is written in the following context

This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

National Institute for Health and Clinical Excellence

MidCity Place
71 High Holborn
London
WC1V 6NA

www.nice.org.uk

Contents

Introduction

Parkinson's disease (PD) is a progressive neurodegenerative condition resulting from the death of the dopamine-containing cells of the substantia nigra. There is no consistently reliable test that can distinguish PD from other conditions that have similar clinical presentations. The diagnosis is primarily clinical, based on a history and examination.

People with PD classically present with the symptoms and signs associated with parkinsonism, namely bradykinesia, rigidity and rest tremor.

Parkinsonism can also be caused by drugs, and conditions that are less common than PD. These include multiple cerebral infarction and degenerative conditions such as progressive supra-nuclear palsy (PSP) and multiple system atrophy (MSA).

Although PD is predominantly a movement disorder, other impairments frequently develop including psychiatric problems such as depression and dementia. Autonomic disturbances and pain (which is rarely a presenting feature of PD) may later ensue, and the condition progresses to cause significant disability and handicap with impaired quality of life for the affected person. Family and carers may also be affected indirectly.

Health and resource implications

PD is a common, chronic, progressive neurological condition, estimated to affect 100–180 people per 100,000 of the population (between 6 and 11 people per 6000 of the general population in the UK)[1] and has an annual incidence of 4–20 per 100,000. There is a rising prevalence with age and a higher prevalence and incidence of PD in males.

[1] The size of the average general practice list in the UK.

Patient-centred care

This guideline offers best practice advice on the care of people with PD and should be read in conjunction with the national service framework (NSF) for long-term (neurological) conditions (2005).

Treatment and care should take into account patients' individual needs and preferences. People with PD should have the opportunity to make informed decisions about their care and treatment. Where patients do not have the capacity to make decisions, healthcare professionals should follow the Department of Health guidelines – 'Reference guide to consent for examination or treatment' (2001).

Good communication between healthcare professionals and patients is essential. It should be supported by the provision of evidence-based information offered in a form that is tailored to the needs of the individual patient. The treatment, care and information provided should be culturally appropriate and in a form that is accessible to people who have additional needs, such as people with physical, cognitive or sensory disabilities, and people who do not speak or read English.

Unless specifically excluded by the patient, carers and relatives should have the opportunity to be involved in decisions about the person's care and treatment.

Carers and relatives should also be provided with the information and support they need.

Key priorities for implementation

The following recommendations have been identified as priorities for implementation.

Referral to expert for accurate diagnosis

- People with suspected PD should be referred quickly[2] and untreated to a specialist with expertise in the differential diagnosis of this condition.

Diagnosis and expert review

- The diagnosis of PD should be reviewed regularly[3] and reconsidered if atypical clinical features develop.

- Acute levodopa and apomorphine challenge tests should not be used in the differential diagnosis of parkinsonian syndromes.

Regular access to specialist nursing care

- 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 carers

  which may be provided by a Parkinson's disease nurse specialist.

[2] The Guideline Development Group considered that people with suspected mild PD should be seen within 6 weeks but new referrals in later disease with more complex problems require an appointment within 2 weeks.

[3] The Guideline Development Group considered that people diagnosed with PD should be seen at regular intervals of 6–12 months to review their diagnosis.

Access to physiotherapy

- Physiotherapy 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.

Access to occupational therapy

- Occupational therapy should be available for people with PD. Particular consideration should be given to:
  - maintenance of work and family roles, employment, 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.

Access to speech and language therapy

- 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 programmes such as Lee Silverman Voice Treatment (LSVT)

- teaching strategies to optimise speech intelligibility
- ensuring an effective means of communication is maintained throughout the course of the disease, including use of assistive technologies
- review and management to support the safety and efficiency of swallowing and to minimise the risk of aspiration.

Palliative care

- Palliative care requirements of people with PD should be considered throughout all phases of the disease.
- People with PD and their carers should be given the opportunity to discuss end-of-life issues with appropriate healthcare professionals.

The following guidance is evidence based. Appendix A shows the grading scheme used for the recommendations: **A**, **B**, **C**, **D** or good practice point – **D(GPP)**. Recommendations on diagnostic test are graded **A(DS)**, **B(DS)**, **C(DS)** or **D(DS)**. A summary of the evidence on which the guidance is based is provided in the full guideline (see section 5).

1 Guidance

1.1 Communication with people with Parkinson's disease and their carers

1.1.1 Communication

1.1.1.1 Communication with people with PD should be aimed towards empowering them to participate in the judgements and choices about their own care. **D**

1.1.1.2 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. **D**

1.1.1.3 Because people with PD may develop impaired cognitive ability, a communication deficit and/or depression, they should be provided with: **D(GPP)**

- both oral and written communication throughout the course of the disease, which should be individually tailored and reinforced as necessary
- consistent communication from the professionals involved.

1.1.1.4 Families and carers should be given information about the condition, their entitlements to care assessment and the support services available. **D(GPP)**

1.1.1.5 People with PD should have a comprehensive care plan agreed between the individual, their family and/or carers and specialist and secondary healthcare providers. **D(GPP)**

1.1.1.6 People with PD should be offered an accessible point of contact with specialist services. This could be provided by a Parkinson's disease nurse specialist. **D(GPP)**

1.1.1.7 All people with PD who drive should be advised to inform the Driver and Vehicle Licensing Agency (DVLA) and their car insurer of their condition at the time of diagnosis. **D(GPP)**

1.2 Diagnosing Parkinson's disease

1.2.1 Definition and differential diagnosis

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

1.2.2 Expert versus non-expert diagnosis

1.2.2.1 People with suspected PD should be referred quickly[4] and untreated to a specialist with expertise in the differential diagnosis of this condition. **B(DS)**

1.2.3 Clinical versus post-mortem diagnosis

1.2.3.1 PD should be diagnosed clinically and based on the UK Parkinson's Disease Society Brain Bank Criteria. **B(DS)**

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

[4] The Guideline Development Group considered that people with suspected mild PD should be seen within 6 weeks, but new referrals in later disease with more complex problems require an appointment within 2 weeks.

1.2.4 Review of diagnosis

1.2.4.1 The diagnosis of PD should be reviewed regularly[5] and re-considered if atypical clinical features develop. **D(DS)**

1.2.5 Single photon emission computed tomography (SPECT)

1.2.5.1 ^{123}I-FP-CIT SPECT should be considered for people with tremor where essential tremor cannot be clinically differentiated from parkinsonism. **A(DS)**

1.2.5.2 ^{123}I-FP-CIT SPECT should be available to specialists with expertise in its use and interpretation. **D(DS)**

1.2.6 Positron emission tomography (PET)

1.2.6.1 PET should not be used in the differential diagnosis of parkinsonian syndromes, except in the context of clinical trials. **B(DS)**

1.2.7 Structural magnetic resonance imaging (MRI)

1.2.7.1 Structural MRI should not be used in the differential diagnosis of Parkinson's disease. **B(DS)**

1.2.7.2 Structural MRI may be considered for the differential diagnosis of parkinsonian syndromes. **D(DS)**

1.2.8 Magnetic resonance volumetry

1.2.8.1 Magnetic resonance volumetry should not be used in the differential diagnosis of parkinsonian syndromes, except in the context of clinical trials. **D(DS)**

1.2.9 Magnetic resonance spectroscopy

1.2.9.1 Magnetic resonance spectroscopy should not be used in the differential diagnosis of parkinsonian syndromes. **B(DS)**

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[5] The Guideline Development Group considered that people diagnosed with PD should be seen at regular intervals of 6–12 months to review their diagnosis.

1.2.10 Acute levodopa and apomorphine challenge tests

1.2.10.1 Acute levodopa and apomorphine challenge tests should not be used in the differential diagnosis of parkinsonian syndromes. **B(DS)**

1.2.11 Objective smell testing

1.2.11.1 Objective smell testing should not be used in the differential diagnosis of parkinsonian syndromes, except in the context of clinical trials. **B(DS)**

1.3 Neuroprotection

1.3.1 Vitamin E

1.3.1.1 Vitamin E should not be used as a neuroprotective therapy for people with PD. **A**

1.3.2 Co-enzyme Q_{10}

1.3.2.1 Co-enzyme Q_{10} should not be used as a neuroprotective therapy for people with PD, except in the context of clinical trials. **B**

1.3.3 Dopamine agonists

1.3.3.1 Dopamine agonists should not be used as neuroprotective therapies for people with PD, except in the context of clinical trials. **B**

1.3.4 Monoamine oxidase B inhibitors

1.3.4.1 Monoamine oxidase B (MAO-B) inhibitors should not be used as neuroprotective therapies for people with PD, except in the context of clinical trials. **B**

1.4 Pharmacological therapy in early PD

In this guideline, 'early disease' refers to PD in people who have developed functional disability and require symptomatic therapy. 'Later disease' refers to PD in people on levodopa who have developed motor complications.

1.4.1 Choice of initial pharmacotherapy in people with early PD

There is no single drug of choice in the initial pharmacotherapy of early PD. Table 1 may help to guide the reader through the following section.

Table 1 Options for initial pharmacotherapy in early PD

Initial therapy for early PD	First-choice option	Symptom control	Risk of side effects	
			Motor complications	Other adverse events
Levodopa	✓	+++	↑	↑
Dopamine agonists	✓	++	↓	↑
MAO-B inhibitors	✓	+	↓	↑
Anticholinergics	×	Lack of evidence	Lack of evidence	Lack of evidence
Beta-blockers	×	Lack of evidence	Lack of evidence	Lack of evidence
Amantadine	×	Lack of evidence	Lack of evidence	Lack of evidence

KEY

+++ = Good degree of symptom control

++ = Moderate degree of symptom control

+ = Limited degree of symptom control

↑ = Evidence of increased motor complications/other adverse events

↓ = Evidence of reduced motor complications/other adverse events

1.4.1.1 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: **D(GPP)**

- 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.

1.4.2 Levodopa

1.4.2.1 Levodopa may be used as a symptomatic treatment for people with early PD. **A**

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

1.4.3 Dopamine agonists

1.4.3.1 Dopamine agonists may be used as a symptomatic treatment for people with early PD. **A**

1.4.3.2 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. **D(GPP)**

1.4.3.3 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.[6] **D(GPP)**

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

1.4.4 Monoamine oxidase B inhibitors

1.4.4.1 MAO-B inhibitors may be used as a symptomatic treatment for people with early PD. **A**

1.4.5 Beta-adrenergic antagonists (beta-blockers)

1.4.5.1 Beta-adrenergi c antagonists may be used in the symptomatic treatment of selected people with postural tremor in PD, but should not be drugs of first choice. **D(GPP)**

[6] Full details of the restrictions on pergolide use and monitoring are available in the 'Summary of product characteristics'.

1.4.6 Amantadine

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

1.4.7 Anticholinergics

1.4.7.1 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. **B**

1.4.8 Modified-release levodopa

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

1.5 Pharmacological therapy in later PD

Most people with PD will develop, with time, motor complications and will eventually require levodopa therapy. Adjuvant drugs to take alongside levodopa have been developed with the aim of reducing these motor complications and improving quality of life.

1.5.1 Choice of adjuvant therapy for people with later PD

There is no single drug of choice in the pharmacotherapy of later PD. Table 2 may help to guide the reader through the following section.

Table 2 Options for adjuvant pharmacotherapy in later PD

Adjuvant therapy for later PD	First-choice option	Symptom control	Risk of side effects	
			Motor complications	Other adverse events
Dopamine agonists	✓	++	↓	↑
COMT inhibitors	✓	++	↓	↑
MAO-B inhibitors	✓	++	↓	↑
Amantadine	✗	NS	↓	↑
Apomorphine	✗	+	↓	↑

KEY

+++ = Good degree of symptom control

++ = Moderate degree of symptom control

+ = Limited degree of symptom control

↑ = Evidence of increased motor complications/other adverse events

↓ = Evidence of reduced motor complications/other adverse events

NS = Non-significant result

1.5.1.1 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: **D(GPP)**

- 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.

1.5.2 Modified-release levodopa

1.5.2.1 Modified-release levodopa preparations may be used to reduce motor complications in people with later PD, but should not be drugs of first choice. **B**

1.5.3 Dopamine agonists

1.5.3.1 Dopamine agonists may be used to reduce motor fluctuations in people with later PD. **A**

1.5.3.2 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[7]. **D(GPP)**

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

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

1.5.4 Monoamine oxidase B inhibitors

1.5.4.1 MAO-B inhibitors may be used to reduce motor fluctuations in people with later PD. **A**

1.5.5 Catechol-O-methyl transferase inhibitors

1.5.5.1 Catechol-O-methyl transferase (COMT) inhibitors may be used to reduce motor fluctuations in people with later PD. **A**

1.5.5.2 In view of problems with reduced concordance, people with later PD taking entacapone should be offered a triple combination preparation of levodopa, carbidopa and entacapone[8]. **D(GPP)**

1.5.5.3 Tolcapone should only be used after entacapone has failed in people with later PD due to lack of efficacy or side effects. Liver function tests are required every 2 weeks during the first year of

[7] Full details of the restrictions on pergolide use and monitoring are available in the 'Summary of product characteristics'.

[8] Trade name Stalevo (Orion)

therapy, and thereafter in accordance with the 'Summary of product characteristics'. **D(GPP)**

1.5.6 Amantadine

1.5.6.1 Amantadine may be used to reduce dyskinesia in people with later PD. **C**

1.5.7 Apomorphine

1.5.7.1 Intermittent apomorphine injections may be used to reduce off time in people with PD with severe motor complications. **B**

1.5.7.2 Continuous subcutaneous infusions of apomorphine may be used to reduce off time and dyskinesia in people with PD with severe motor complications. Its initiation should be restricted to expert units with facilities for appropriate monitoring. **D**

1.6 Further drug administration considerations

1.6.1.1 Antiparkinsonian 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. **D(GPP)**

1.6.1.2 The practice of withdrawing patients from their antiparkinsonian drugs (so called 'drug holidays') to reduce motor complications should not be undertaken because of the risk of neuroleptic malignant syndrome. **D(GPP)**

1.6.1.3 In view of the risks of sudden changes in antiparkinsonian medication, people with PD who are admitted to hospital or care homes should have their medication: **D(GPP)**

- given at the appropriate times, which in some cases may mean allowing self-medication.
- adjusted by, or adjusted only after discussion with, a specialist in the management of PD.

1.6.1.4 Clinicians should be aware of dopamine dysregulation syndrome, 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. **D(GPP)**

1.7 Surgery for Parkinson's disease

NICE has also published interventional procedure guidance 'Deep brain stimulation for Parkinson's disease'. Available from www.nice.org.uk/IPG019

1.7.1 Subthalamic nucleus stimulation

1.7.1.1 Bilateral subthalamic nucleus (STN) stimulation may be used in people with PD who: **D**

- have motor complications that are refractory to best medical treatment,
- are biologically fit with no clinically significant active comorbidity,
- are levodopa responsive and
- have no clinically significant active mental health problems, for example, depression or dementia.

1.7.2 Globus pallidus interna stimulation

1.7.2.1 Bilateral globus pallidus interna (GPi) stimulation[9] may be used in people with PD who: **D(GPP)**

- have motor complications that are refractory to best medical treatment,
- are biologically fit with no clinically significant active comorbidity,
- are levodopa responsive and
- have no clinically significant active mental health problems, for example, depression or dementia.

[9] GPi deep brain stimulation is rarely performed for PD in the UK at present, though it is sometimes undertaken when STN deep brain stimulation is not possible.

1.7.3 Comparison of STN and GPi stimulation

1.7.3.1 With the current evidence it is not possible to decide if the subthalamic nucleus or globus pallidus interna is the preferred target for deep brain stimulation 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: **D(GPP)**

- clinical and lifestyle characteristics of the person with PD
- patient preference, after the patient has been being informed of the potential benefits and drawbacks of the different surgical procedures.

1.7.4 Thalamic stimulation

1.7.4.1 Thalamic deep brain stimulation may be considered as an option in people with PD who predominantly have severe disabling tremor and where STN stimulation cannot be performed. **D**

1.8 Non-motor features of Parkinson's disease

1.8.1 Mental health problems

Depression

1.8.1.1 Clinicians should have a low threshold for diagnosing depression in PD. **D(GPP)**

1.8.1.2 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. **D(GPP)**

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

Psychotic symptoms

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

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

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

1.8.1.7 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. **D(GPP)**

1.8.1.8 Atypical antipsychotics may be considered for treatment of psychotic symptoms in people with PD, although the evidence base for their efficacy and safety is limited. **D(GPP)**

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

Dementia

1.8.1.10 Although cholinesterase inhibitors have been used successfully in individual people with PD dementia, further research is recommended to identify those patients who will benefit from this treatment. **D(GPP)**

1.8.2 Sleep disturbance

1.8.2.1 A full sleep history should be taken from people with PD who report sleep disturbance. **D(GPP)**

1.8.2.2 Good sleep hygiene should be advised in people with PD with any sleep disturbance and includes: **D(GPP)**

- 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, H_2 antagonists, antipsychotics and sedatives).

1.8.2.3 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. **D(GPP)**

1.8.2.4 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. **D(GPP)**

Daytime hypersomnolence

1.8.2.5 Modafinil may be considered for daytime hypersomnolence in people with PD. **D(GPP)**

Nocturnal akinesia

1.8.2.6 Modified-release levodopa preparations may be used for nocturnal akinesia in people with PD. **D(GPP)**

1.8.3 Falls

1.8.3.1 For all people with PD at risk of falling, please refer to 'Falls: assessment and prevention of falls in older people' *NICE clinical guideline* no. 21
(available from www.nice.org.uk/CG021) **NICE 2004**

1.8.4 Autonomic disturbance

1.8.4.1 People with PD should be treated appropriately for the following autonomic disturbances[10]: **D(GPP)**

- urinary dysfunction
- weig ht loss
- dysphagia
- constipation
- erectile dysfunction
- orthostatic hypotension
- excess ive sweating
- sialorrhoea.

1.9 Other key interventions

1.9.1 Specialist nurse interventions

1.9.1.1 People with PD should have regular access to the following: **C**

- 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 carers

which may be provided by a Parkinson's disease nurse specialist.

[10] Please refer to the full Parkinson's disease guideline for additional information.

1.9.2 Physiotherapy

1.9.2.1 Physiotherapy should be available for people with PD. Particular consideration should be given to: **B**

- 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.

1.9.2.2 The Alexander Technique may be offered to benefit people with PD by helping them to make lifestyle adjustments that affect both the physical nature of the condition and the person's attitudes to having PD. **C**

1.9.3 Occupational therapy

1.9.3.1 Occupational therapy should be available for people with PD. Particular consideration should be given to: **D(GPP)**

- 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.

1.9.4 Speech and language therapy

1.9.4.1 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 programmes such as Lee Silverman Voice Treatment (LSVT) **B**
- teaching strategies to optimise speech intelligibility **D(GPP)**
- ensuring an effective means of communication is maintained throughout the course of the disease, including use of assistive technologies **D(GPP)**
- review and management to support safety and efficiency of swallowing and to minimise the risk of aspiration. **D(GPP)**

1.10 Palliative care in Parkinson's disease

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

1.10.1.2 People with PD and their carers should be given the opportunity to discuss end-of-life issues with appropriate healthcare professionals. **D(GPP)**

2 Notes on the scope of the guidance

All NICE guidelines are developed in accordance with a scope document that defines what the guideline will and will not cover. The scope of this guideline was established, after a period of consultation, at the start of the guideline development process; it is available from www.nice.org.uk/page.aspx?o=213723.

This guideline sets out best practice guidance for the diagnosis and management of PD in the NHS in England and Wales. Guidance covers primary, secondary and tertiary healthcare settings. It applies to men and women older than 20 years of age, with a diagnosis of Parkinson's disease or parkinsonism. The guidance on treatment and management is aimed at

people with idiopathic Parkinson's disease only. The following areas are covered in this guideline:

- diagnosis and monitoring
- communication and education
- pharmacotherapy (prevention of progression)
- pharmacotherapy (functional disability in early disease)
- adjuvant pharmacotherapy (functional disability in late disease)
- non-pharmacological management
- neuropsychiatric conditions
- palliative care.

This guideline does not cover other therapies that do not form common clinical management (such as fetal cell transplantation; stem cells; genes that code proteins responsible for producing dopamine; drugs that block the action of glutamate; glial cell-derived neurotrophic factor [GDNF]; and viral transfection). In addition, comorbidities in Parkinson's disease are not addressed (except where treatment differs from treatment of these comorbidities in patients without Parkinson's disease). Finally, generic health problems where the care for people with Parkinson's disease does not differ to that of the general population (such as constipation) are not addressed.

3 Implementation in the NHS

The Healthcare Commission will assess the performance of NHS organisations in meeting core and developmental standards set by the Department of Health in 'Standards for better health' issued in July 2004.

Implementation of clinical guidelines forms part of the developmental standard D2. Core standard C5 says that national agreed guidance should be taken into account when NHS organisations are planning and delivering care.

This guideline is supported by the following implementation tools available on our website www.nice.org.uk/CG035

- A slide set – key messages for local discussion.
- Costing tools:
  – a national costing report, which estimates the overall resource impact associated with implementation
  – a local costing template; a simple spreadsheet that can be used to estimate the local cost of implementation.
- Implementation advice – practical suggestions on how to address potential barriers to implementation.

Suggested audit criteria based on the key priorities for implementation are listed in appendix D of this document (see page 42) and can be used to audit practice locally.

4 Research recommendations

The Guideline Development Group has made the following recommendations for research on the basis of its review of the evidence. The Group regards these recommendations as the most important research areas to improve NICE guidance and patient care in the future. The Guideline Development Group's full set of research recommendations is detailed in the full guideline (see section 5).

4.1 Neuroprotection

Do any of the agents with preclinical neuroprotective properties in PD models have any clinically worthwhile protective effects in PD?

Why this is important

At present there is no agent that slows down the progression of PD. Patients want such a 'cure' for their condition. The NHS requires neuroprotectants to reduce the burden of disability caused by PD, thereby reducing the direct and indirect costs of caring for an increasing number of people with the condition.

A systematic trial programme examining these agents is ongoing in the USA (NET-PD). Agents are being screened in small 'futility studies' using historical control data for decline in total UPDRS scores. The first futility study showed that both minocycline and GPi 1485 significantly delay decline in total UPDRS by more than 30% (K Kieburtz, personal communication).

The recent rasagiline delayed-start design trial versus placebo raised the possibility that this may be a useful trial design to examine neuroprotection. Support for further surgical approaches to neuroprotection in PD should be considered.

4.2 Dementia

Which people with PD and dementia benefit from cholinesterase inhibitors and/or memantine, and is the use of these agents cost effective?

Why this is important

A recent systematic review indicated that 24–31% of patients with PD have dementia, and that 3–4% of the dementia in the general population is due to Parkinson's disease dementia (PDD). The estimated prevalence of PDD in the general population aged 65 years and older is 0.2–0.5%. PDD is associated with increased mortality, care-giver stress and nursing home admission.

A large randomised controlled trial (RCT) of rivastigmine in PDD showed improvements in primary and secondary end points, but the clinical significance of these benefits is uncertain. It is likely that the modest mean

improvements reflect heterogeneity of response, with some patients responding far better than others; this is supported by expert opinion via open-label prescribing. In addition, health economics analyses have not been performed in trials of cholinesterase inhibitors in PDD using disease-specific models.

Identifying responsive subgroups of patients with PDD with demonstrable cost effectiveness would focus effective targeting of cholinesterase inhibitors and/or memantine. The process of identifying these patients would also lead to the development of protocols for prescribing and assessment, together with robust guidelines regarding whether drug usage is maintained or discontinued.

4.3 Depression

Is treating mild to moderate depression in PD with an antidepressant cost effective?

Why this is important

Cross-sectional studies have shown that depression affects around 40% of patients with PD and has a major impact on quality of life. In most cases, depression is mild to moderate in severity and is often missed by the clinician caring for the patient.

The GDG recommends a study that would screen secondary care Parkinson's disease clinic populations for mild to moderate depression. Participants would then be treated with any SSRI class antidepressant or no such treatment in an open-label fashion. This would be a large-scale pragmatic trial.

If screening for and treating mild to moderate depression is cost effective, this would add to the evidence base for the management of depression in Parkinson's disease and may have considerable impact on the next update of this guideline.

4.4 Supportive therapies

4.4.1 Physiotherapy

Is physiotherapy in PD cost effective?

Why this is important

The evidence to support the use of physiotherapy in Parkinson's disease is limited and yet patients feel that it is effective. Many patients are referred for such therapy in the NHS with little idea of its value or whether it has any long-term benefits. In contrast, many other patients cannot access such therapy due to limited provision of service.

The GDG recommends a pragmatic trial should be performed in units that already have access to physiotherapy services. This is likely to be in the elderly care setting because neurologists have limited access to such treatments.

If physiotherapy is cost effective then the provision of service needs to be increased.

Future trials will then need to examine which components of physiotherapy are effective and whether it is effective in the earlier stages of the disease.

4.4.2 Occupational therapy

Is occupational therapy in PD cost effective?

Why this is important

The evidence to support the use of occupational therapy in PD is limited and yet patients feel that it is effective. Many patients are referred for such therapy in the NHS with little idea of its value or whether it has any long-term benefits. In contrast, many other patients cannot access such therapy due to limited provision of service.

The GDG recommends a pragmatic trial should be performed in units that already have access to occupational therapy services. This is likely to be in

the elderly care setting because neurologists have poor access to such treatments.

If occupational therapy is cost effective then the provision of service needs to be increased.

Future trials will then need to examine what components of occupational therapy are effective and whether it is effective in the earlier stages of the disease.

4.4.3 Speech and language therapy

Is NHS speech and language therapy in PD cost effective?

Why this is important

The evidence to support the use of speech and language therapy in PD is limited and yet patients feel that it is effective. The provision of this service in the NHS is patchy with some patients not receiving speech and language therapy when it may be appropriate.

The GDG recommends a trial that is preceded by survey work to identify current and best practice speech and language therapy for PD in the UK. Similar work has already been performed for physiotherapy and occupational therapy to prepare for analogous trials.

In this pragmatic trial, standard NHS speech and language therapy would be compared with no treatment. Whilst most PD units have access to some speech and language therapy service, this may be insufficient for trial purposes so an NHS subvention would be required.

If speech and language therapy is cost effective, then the provision of service needs to be increased.

4.5 Diagnostic investigations

Which diagnostic investigations for PD and potential biomarkers of its progression are clinically useful and cost effective?

Why this is important

The diagnosis of PD remains clinical. ^{123}I-FP-CIT SPECT may be of additional help in a small proportion of clinically uncertain cases. The diagnostic error rate on presentation may be as high as 10% in expert hands, which may lead to inappropriate therapy and distress following revision of the diagnosis.

A systematic approach would expedite the evaluation of existing and new diagnostic techniques.

The considerable debate surrounding biomarkers to measure the progression of PD has highlighted the need for further studies in this area. More work on existing techniques (for example, SPECT and PET) is required and the development of new potential markers of progression is urgently required.

5 Other versions of this guideline

The National Institute for Health and Clinical Excellence commissioned the development of this guidance from the National Collaborating Centre for Chronic Conditions. The Centre established a Guideline Development Group, which reviewed the evidence and developed the recommendations. The members of the Guideline Development Group are listed in appendix B. Information about the independent Guideline Review Panel is given in appendix C.

The booklet 'The guideline development process: an overview for stakeholders, the public and the NHS' has more information about the Institute's guideline development process. It is available from www.nice.org.uk/guidelinesprocess.

5.1 Full guideline

The full guideline, 'Parkinson's disease: diagnosis and management in primary and secondary care', is published by the National Collaborating Centre for Chronic Conditions; it is available from the RCP website (www.rcplondon.ac.uk/pubs/books/PD), the NICE website (www.nice.org.uk/CG035fullguideline) and the website of the National Library for Health (www.nlh.nhs.uk).

5.3 Information for the public

NICE has produced information for the public explaining this guideline. We encourage NHS and voluntary sector organisations to use text from this information in their own materials.

6 Related NICE guidance

Depression: management of depression in primary and secondary care. *NICE clinical guideline* no. 23 (2004). Available from www.nice.org.uk/CG023

Falls: The assessment and prevention of falls in older people. *NICE clinical guideline* no. 21(2004). Available from www.nice.org.uk/CG021

Nutrition support in adults: oral nutrition support, enteral tube feeding and parenteral nutrition. *NICE clinical guideline* No. 32(2006). Available from www.nice.org.uk/CG032

Alzheimer's disease – donepezil, rivastigmine and galantamine. *NICE technology appraisal* no. 19 (2001). Available from www.nice.org.uk/TA019 (this is currently under review, see page 34)

Deep brain stimulation for Parkinson's disease. *NICE interventional procedure guidance* no 19 (2003). Available from www.nice.org.uk/IPG019

NICE is in the process of developing the following guidance (details available from www.nice.org.uk):

- Dementia: management of dementia, including use of antipsychotic medication in older people. *NICE clinical guideline.* (Publication expected February 2007)
- Donepezil, rivastigmine, galantamine and mementine for the treatment of Alzheimer's disease (including a review of existing guidance no. 19) *NICE technology appraisal.* (Publication expected late 2006.)

7 Review date

The process of reviewing the evidence is expected to begin 4 years after the date of issue of this guideline. Reviewing may begin before this if significant evidence that affects the guideline recommendations is identified. The updated guideline will be available within 2 years of the start of the review process.

Appendix A: Grading scheme

The classification of recommendations and the levels of evidence for intervention studies used in this guideline are adapted from the Scottish Intercollegiate Guidelines Network ('SIGN 50: a guideline developers' handbook'), and are summarised in the tables below and on page 36. The classification of recommendations and levels of evidence for the accuracy of diagnostic tests are adapted from 'The Oxford centre for evidence-based medicine levels of evidence' (2001) and the 'Centre for reviews and dissemination report no. 4' (2001). They are summarised in the tables on pages 36 and 37 and are being used on a pilot basis.

Classification of recommendations on interventions

Recommendation grade	Evidence
A	• At least one meta-analysis, systematic review, or randomised controlled trial (RCT) that is rated as 1^{++}, and is directly applicable to the target population, **or** • A systematic review of RCTs or a body of evidence that consists principally of studies rated as 1+, is directly applicable to the target population and demonstrates overall consistency of results, **or** • Evidence drawn from a NICE technology appraisal
B	• A body of evidence that includes studies rated as 2^{++}, is directly applicable to the target population and demonstrates overall consistency of results, **or** • Extrapolated evidence from studies rated as 1^{++} or 1^{+}
C	• A body of evidence that includes studies rated as 2^{+}, is directly applicable to the target population and demonstrates overall consistency of results, **or** • Extrapolated evidence from studies rated as 2^{++}
D	• Evidence level 3 or 4, **or** • Extrapolated evidence from studies rated as 2^{+}, **or** • Formal consensus
D(GPP)	• A good practice point (GPP) is a recommendation for best practice based on the experience of the Guideline Development Group

Levels of evidence for intervention studies

Level of evidence	Type of evidence
1^{++}	• High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1^{+}	• Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1^{-}	• Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2^{++}	• High-quality systematic reviews of case–control or cohort studies • High-quality case–control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal
2^{+}	• Well-conducted case–control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal
2^{-}	• Case–control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal
3	• Non-analytical studies (for example, case reports, case series)
4	• Expert opinion, formal consensus

Classification of recommendations on diagnostic tests

Grade	Evidence
A(DS)	• Studies with level of evidence Ia or Ib
B(DS)	• Studies with level of evidence II
C(DS)	• Studies with level of evidence III
D(DS)	• Studies with level of evidence IV

DS, diagnostic studies.

Levels of evidence for studies of the accuracy of diagnostic tests

Levels of evidence	Type of evidence
Ia	• Systematic review (with no or minor variations in the directions and degrees of results between studies) of level-1 studies, which are studies that use: – a blind comparison of the test with a validated reference standard (gold standard) – a sample of patients that reflects the population to whom the test would apply
Ib	• Level-1 studies
II	• Level-2 studies, which are studies that have only one of the following: – the population is narrow (the sample does not reflect the population to whom the test would apply) – a poor reference standard is used (defined as that where the 'test' is included in the 'reference', or where the 'testing' affects the 'reference') – the comparison between the test and reference standard is not blind – the study is a case–control study • Systematic reviews of level-2 studies
III	• Level-3 studies, which are studies that have at least two of the features listed for level-2 studies • Systematic reviews of level-3 studies
IV	• Consensus, expert committee reports or opinions and/or clinical experience without explicit critical appraisal; or based on physiology, bench research or 'first principles'

Appendix B: The Guideline Development Group

Professor David Anderson

Consultant Psychiatrist, Mossley Hill Hospital, Liverpool

Ms Angela Birleson

Advanced Practitioner in Occupational Therapy, Occupational Therapy, Clinical Support Services, South Tees Hospitals NHS Trust

Dr David Burn

Consultant Neurologist, Newcastle General Hospital, Newcastle-upon-Tyne

Dr Carl Clarke

Clinical Advisor, City Hospital and University of Birmingham

Ms Bernadette Ford

Information Scientist, NCC-CC

Mr Michael Godfrey

Patient Representative, Parkinson's Disease Society

Ms Jacqui Handley

Parkinson's Disease Nurse Specialist, Dorset County Hospital, Dorchester

Dr John Hindle

Consultant Physician, Care of the Elderly, North West Wales NHS Trust, Bangor

Professor Brian Hurwitz

General Practitioner, King's College London

Professor Andrew Lees

Professor of Neurology, Reta Lila Weston Institute of Neurological Studies, Institute of Neurology, University College London

Dr Alastair Mason

GDG Chair, NCC-CC

Dr Doug MacMahon

Consultant Physician (with special responsibility for the elderly), Royal Cornwall Hospitals NHS Trust

Mr David McNiven

Policy and Campaigns Manager, Parkinson's Disease Society

Mr Robert Meadowcroft

Director of Policy, Campaigns and Information, Parkinson's Disease Society

Ms Debbie Nicholl

Health Economist, NCC-CC

Ms Jill Parnham

Senior Research Fellow, NCC-CC

Ms Bhanu Ramaswamy

Consultant Physiotherapist, Walton Hospital, Chesterfield

Ms Tara Sullivan

Research Fellow and Project Manager, NCC-CC

Ms Nicole Wilson

Project Manager, NCC-CC

Julia Johnson

Speech and Language Therapist, Kings College Hospital, London

TRK Varma

Consultant Neurosurgeon, Walton Centre for Neurology and Neurosurgery, Liverpool

Ana Aragon

Specialist Occupational Therapist for Parkinson's Disease, Bath and North East Somerset Primary Care Trust

Ira Leroi

Consultant in Old Age Psychiatry, Manchester Mental Health and Social Care Trust

Karen Durrant

Superintendent Physiotherapist, Walton Hospital, Chesterfield

David Stewart

Consultant Physician, Medicine for the Elderly, Mansion House Unit, Victoria Infirmary, Glasgow

Appendix C: The Guideline Review Panel

The Guideline Review Panel is an independent panel that oversees the development of the guideline and takes responsibility for monitoring its quality. The Panel includes experts on guideline methodology, health professionals and people with experience of the issues affecting patients and carers. The members of the Guideline Review Panel were as follows.

Dr Peter Rutherford (Chair)
Senior Lecturer in Nephrology, University of Wales College of Medicine

Dame Helena Shovelton
Chief Executive, British Lung Foundation

Dr Rob Higgins
Consultant in Renal and General Medicine, University Hospitals Coventry and Warwickshire NHS Trust, Coventry

Dr John Young
Medical Director, Merck Sharp & Dohme (MSD)

Appendix D: Technical detail on the criteria for audit

The GDG recommends that healthcare-commissioning organisations survey the views of people with PD regarding patient views. This approach would enable the organisations to investigate the totality of the services and identify particular areas in need of development using a patient-centred approach.

Criterion	Exception	Definition of terms
1. 100% of people with suspected Parkinson's disease are seen within 6 weeks of GP referral.	None None	
2. 100% of people with Parkinson's disease are reviewed at 6- to 12-month intervals.	None None	
3. 0% of people with suspected PD are offered acute levodopa and/or apomorphine challenge tests for the differential diagnosis of parkinsonian syndromes.	None None	
4. 100% of people with Parkinson's disease have access to a Parkinson's disease nurse specialist or other professional capable of providing: • 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 carers.	None None	
5. For 100% of people with Parkinson's disease, at diagnosis and each regular review, physiotherapy is available and appropriate referral is activated. This is recorded in the patient's notes.	None None	
6. For 100% of people with Parkinson's disease, at diagnosis and each regular review, occupational therapy is available and appropriate referral is activated. This is recorded in the patient's notes.	None None	
7. For 100% of people with Parkinson's disease, at diagnosis and each regular review, speech and language therapy is available	None None	

and appropriate referral is activated. This is recorded in the patient's notes.		
8. 100% of people with PD should be given opportunities to discuss and ask questions about their palliative care requirements with appropriate healthcare professionals.	None None	

Appendix E: Algorithm