



## Complete Summary

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### GUIDELINE TITLE

Parkinson's disease. National clinical guideline for diagnosis and management in primary and secondary care.

### BIBLIOGRAPHIC SOURCE(S)

National Collaborating Centre for Chronic Conditions. Parkinson's disease. National clinical guideline for diagnosis and management in primary and secondary care. London (UK): Royal College of Physicians; 2006. 237 p. [418 references]

### GUIDELINE STATUS

This is the current release of the guideline.

## \*\* REGULATORY ALERT \*\*

### FDA WARNING/REGULATORY ALERT

**Note from the National Guideline Clearinghouse:** This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [March 29, 2007, Permax \(pergolide\)](#): Voluntary market withdrawal in the U.S. and worldwide due to safety concerns of an increased risk of cardiovascular events. See the U.S. Food and Drug Administration (FDA) Web site for more information.

## COMPLETE SUMMARY CONTENT

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## SCOPE

### **DISEASE/CONDITION(S)**

Parkinson's disease

### **GUIDELINE CATEGORY**

Diagnosis  
Evaluation  
Management  
Treatment

### **CLINICAL SPECIALTY**

Family Practice  
Geriatrics  
Internal Medicine  
Neurological Surgery  
Neurology  
Nursing  
Physical Medicine and Rehabilitation  
Psychiatry  
Speech-Language Pathology

### **INTENDED USERS**

Advanced Practice Nurses  
Allied Health Personnel  
Health Care Providers  
Hospitals  
Nurses  
Occupational Therapists  
Patients  
Physical Therapists  
Physicians  
Public Health Departments  
Social Workers  
Speech-Language Pathologists

### **GUIDELINE OBJECTIVE(S)**

To provide a user-friendly, clinical evidence-based guideline for the National Health Service (NHS) in England and Wales that:

- Offers best clinical advice for Parkinson's disease (PD)
- Is based on best published evidence and expert consensus
- Takes into account patient choice and informed decision making
- Defines the major components of NHS care provision for PD
- Indicates areas suitable for clinical audit
- Details areas of uncertainty or controversy requiring further research

- Provides a choice of guideline versions for different audiences

## **TARGET POPULATION**

Adults (age over 20 years) who are suspected of having, or are diagnosed with, Parkinson's disease (PD) and parkinsonism (Note: Parkinsonism is considered for diagnosis only)

The scope excludes:

- Juvenile onset PD (in people younger than 20 years of age)
- Pregnant women
- Treatment of parkinsonism (a neurological disorder that manifests with hypokinesia, tremor or muscular rigidity) and other tremulous disorders (for example, essential tremor)

## **INTERVENTIONS AND PRACTICES CONSIDERED**

### **Diagnosis/Evaluation**

1. Clinical expert diagnosis using UK Parkinson's Disease Society criteria
2. Differential diagnosis
3. Clinical versus post-mortem diagnosis
4. Regular review of diagnosis
5. Magnetic resonance imaging
6. Single photon emission computed tomography

### **Treatment/Management**

1. Symptomatic pharmacological therapy
  - Levodopa
  - Dopamine agonists
  - Monoamine oxidase type B (MAOB) inhibitors
  - Beta-adrenergic antagonists (beta-blockers)
  - Amantadine
  - Anticholinergics
  - Apomorphine
  - Catechol-O-methyl-transferase inhibitors
2. Surgery
  - Subthalamic nucleus stimulation
  - Globus pallidus interna stimulation
  - Thalamic stimulation
3. Treatment of non-motor features of Parkinson's disease including
  - Depression
  - Psychotic symptoms
  - Dementia
  - Sleep disturbance
  - Daytime hypersomnolence
  - Nocturnal akinesia
  - Falls
  - Autonomic disturbances

- Pain
- 4. Parkinson's disease nurse specialist care
- 5. Physiotherapy
- 6. Occupational therapy
- 7. Speech and language therapy
- 8. Communication with patients and carers
- 9. Patient education

**Note:** Interventions and practices considered but not recommended include: objective smell testing, acute levodopa and apomorphine challenge tests, magnetic resonance spectroscopy, magnetic resonance volumetry, positron emission tomography, vitamin E, and co-enzyme Q10.

## **MAJOR OUTCOMES CONSIDERED**

- Quality of life
- Symptom control
- Specificity and sensitivity of diagnostic tests
- Mortality rate
- Adverse effects associated with treatment
- Motor outcomes

## **METHODOLOGY**

### **METHODS USED TO COLLECT/SELECT EVIDENCE**

Hand-searches of Published Literature (Primary Sources)  
 Hand-searches of Published Literature (Secondary Sources)  
 Searches of Electronic Databases

### **DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE**

#### **Searching the Evidence**

The information scientist developed a search strategy for each clinical question. In addition, the health economist searched for supplemental papers to inform models. Key words for the search were identified by the Guideline Development Group (GDG). Papers that were published or accepted for publication in peer reviewed journals were considered as evidence by the GDG. Conference paper abstracts and non-English language papers were excluded from all searches.

Each clinical question dictated the appropriate study design that was prioritised in the search strategy, but the strategy was not limited solely to these study types. The research fellow or health economist identified titles and abstracts from the search results that appeared to be relevant to the question. Exclusion lists were generated for each question together with the rationale for the exclusion. The exclusion lists were presented to the GDG. Full papers were obtained where relevant. Literature search details are shown in Appendix B of the original guideline document.

#### **Appraising the Evidence**

The research fellow or health economist, as appropriate, critically appraised the full papers. In general no formal contact was made with authors; however, there were ad hoc occasions when this was required in order to clarify specific details. Critical appraisal checklists were compiled for each full paper. One research fellow undertook the critical appraisal and data extraction. The evidence was considered carefully by the GDG for accuracy and completeness.

All procedures are fully compliant with the:

- National Institute for Health and Clinical Excellence (NICE) methodology as detailed in Guideline development methods – information for National Collaborating Centres and guideline developers' manual
- National Collaborating Centres-Chronic Conditions (NCC-CC) quality assurance document and systematic review chart.

### **Health Economics Evidence**

After agreement and selection of specific areas, the information scientist performed a literature search using economic filters on the related clinical questions. No study design criteria were imposed a priori. The searches were not limited to randomised controlled trials (RCTs) or formal economic evaluations. See the earlier section on 'Searching for the evidence' for details of the systematic search by the information scientist. The health economist reviewed titles and abstracts identified in the economic searches, and full papers were obtained as appropriate. The health economist critically appraised the full papers and the relevant data were presented to the GDG at subsequent GDG meetings. See the previous section for information on critically appraising the evidence.

The health economist performed supplemental literature searches using key search terms in the York Centre for Review and Dissemination database, the National Health Service (NHS) Economic Evaluation database, PubMed and the Google search engine to obtain additional information for modelling. Areas were modelled due to the limited amount of evidence in or relevance to the UK setting. Assumptions and designs of the models were explained and agreed by the GDG members during meetings and validated by an additional health economist.

### **NUMBER OF SOURCE DOCUMENTS**

Not stated

### **METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE**

Weighting According to a Rating Scheme (Scheme Given)

### **RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE**

#### **Levels of Evidence for Intervention Studies**

**1++** High quality meta-analysis (MA), systematic reviews (SR) of randomised controlled trials (RCTs), or RCTs with a very low risk of bias

**1+** Well conducted MA, SR or RCTs, or RCTs with a low risk of bias

**1-** MA, SR of RCTs, or RCTs with a high risk of bias

**2++** High quality SR 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-analytic studies (for example, case reports, case series)

**4** Expert opinion, formal consensus

### **Levels of Evidence for Studies of the Accuracy of Diagnostic Tests**

**Ia** Systematic review (with homogeneity)\* of level-1 studies\*\*

**Ib** Level-1 studies\*\*

**II** Level-2 studies\*\*\*

Systematic reviews of level-2 studies

**III** Level-3 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'

\*Homogeneity means there are no or minor variations in the directions and degrees of results between individual studies that are included in the systematic review.

\*\*Level-1 studies are studies:

- That use a blind comparison of the test with a validated reference standard (gold standard)
- In a sample of patients that reflects the population to whom the test would apply.

\*\*\*Level-2 studies are studies that have **only one** of the following:

- Narrow population (the sample does not reflect the population to whom the test would apply)
- Use a poor reference standard (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
- Case-control studies

\*\*\*\*Level-3 studies are studies that have **at least two or three** of the features listed for level-2 studies.

## **METHODS USED TO ANALYZE THE EVIDENCE**

Review of Published Meta-Analyses  
Systematic Review with Evidence Tables

## **DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE**

### **Distilling and Synthesising the Evidence**

The evidence from each full paper was distilled into an evidence table and synthesised into evidence statements before being presented to the Guideline Development Group (GDG). This evidence was then reviewed by the GDG and used as a basis upon which to formulate recommendations.

Evidence tables are available at:

<http://www.rcplondon.ac.uk/pubs/evidencetables/e34/index.htm>.

## **METHODS USED TO FORMULATE THE RECOMMENDATIONS**

Expert Consensus

## **DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS**

### **Agreeing the Recommendations**

The sign-off workshop employed formal consensus techniques to:

- Ensure that the recommendations reflected the evidence base
- Approve recommendations based on lesser evidence or extrapolations from other situations
- Reach consensus recommendations where the evidence was inadequate
- Debate areas of disagreement and finalise recommendations

The sign-off workshop also reached agreement on the following:

- Five to ten key priorities for implementation
- Five key research recommendations
- Algorithms

In prioritising key recommendations for implementation, the sign-off workshop also took into account the following criteria:

- High clinical impact
- High impact on reducing variation
- More efficient use of National Health Service (NHS) resources
- Allowing the patient to reach critical points in the care pathway more quickly

The audit criteria provide suggestions of areas for audit in line with the key recommendations for implementation.

## **Writing the Guideline**

The first draft version of the guideline was drawn up by the Technical Team in accord with the decision of the Guideline Development Group.

## **RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS**

### **Classification of Recommendations**

#### **Grade A:**

- Level 1++ and directly applicable to the target population, or
- Level 1+ and directly applicable to the target population AND consistency of results
- Evidence from National Institute for Health and Clinical Excellence (NICE) technology appraisal

#### **Grade B:**

- Level 2 ++, directly applicable to the target population and demonstrating overall consistency of results, or
- Extrapolated evidence from studies rated as 1++ or 1+

#### **Grade C:**

- Level 2+, directly applicable to the target population and demonstrating overall consistency of results, or
- Extrapolated evidence from studies rated as 2++

#### **Grade D:**

- Level 3 or 4, or
- Extrapolated from 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

### **Grading of Recommendations on Diagnostic Tests**

**Grade A (DS)** Studies with level of evidence Ia or Ib

**Grade B (DS)** Studies with level of evidence II

**Grade C (DS)** Studies with level of evidence III

**Grade D (DS)** Studies with level of evidence IV

(DS, diagnostic studies)

## **COST ANALYSIS**

Due to the appointment of the health economist midway through the guideline development, the areas for health economic evidence were considered after the formation of the clinical questions.

The health economist reviewed the clinical questions to consider the potential application of health economic evidence. Five key areas were separately identified by the clinical lead.

Details of the economic analysis are found in the original full-length guideline document.

## **METHOD OF GUIDELINE VALIDATION**

External Peer Review  
Internal Peer Review

## **DESCRIPTION OF METHOD OF GUIDELINE VALIDATION**

The guideline was validated through two consultations.

1. The first draft of the guideline (The full guideline, National Institute for Clinical Excellence [NICE] guideline and Quick Reference Guide) were consulted with Stakeholders and comments were considered by the Guideline Development Group (GDG)
2. The final consultation draft of the Full guideline, the NICE guideline and the Information for the Public were submitted to stakeholders for final comments.

The final draft was submitted to the Guideline Review Panel for review prior to publication.

# **RECOMMENDATIONS**

## **MAJOR RECOMMENDATIONS**

The strength of recommendation grading (A–D (GPP)) and level of evidence (1++-4) for interventional studies and strength of recommendation grading A (DS)– D (DS) and level of evidence (Ia–IV) for diagnostic studies are defined at the end of the "Major Recommendations" field.

In addition to evidence-based recommendations, the guideline development group (GDG) also identifies evidence from the National Institute for Health and Clinical Excellence (NICE) guidelines or health technology appraisal programme (NICE).

## **Communication with People with Parkinson's Disease (PD) and Their Carers**

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

**D** - 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 (GPP)** - 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
- Consistent communication from the professionals involved

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

**D (GPP)** - 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)** - 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)** - 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.

## **Diagnosing Parkinson's Disease**

### **Definition and Differential Diagnosis**

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

### **Clinical Versus Post-Mortem Diagnosis**

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

(See Table 5.1 "UK PDS Brain Bank Criteria for the diagnosis of PD" in the original full-length guideline document.)

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

### **Expert Versus Non-Expert Diagnosis**

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

\*The GDG 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.

### **Review of Diagnosis**

**D (DS)** - The diagnosis of PD should be reviewed regularly\*\* and reconsidered if atypical clinical features develop.

\*\*The GDG considered that people diagnosed with PD should be seen at regular intervals of 6–12 months to review their diagnosis.

### **Single Photon Emission Computed Tomography (SPECT)**

**A (DS)** -  $^{123}\text{I}$ -FP-CIT [(N-omega-fluoropropyl-2beta-carboxymethoxy-3beta-(4-iodophenyl)tropane)] SPECT should be considered for people with tremor where essential tremor cannot be clinically differentiated from parkinsonism.

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

### **Positron Emission Tomography (PET)**

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

### **Magnetic Resonance Imaging (MRI)**

**B (DS)** - Structural MRI should not be used in the differential diagnosis of PD.

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

### **Magnetic Resonance Volumetry**

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

### **Magnetic Resonance Spectroscopy**

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

### **Acute Levodopa and Apomorphine Challenge Tests**

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

## **Objective Smell Testing**

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

## **Neuroprotection**

### **Vitamin E**

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

### **Co-enzyme Q<sub>10</sub>**

**B** - Co-enzyme Q<sub>10</sub> should not be used as a neuroprotective therapy for people with PD, except in the context of clinical trials.

### **Dopamine Agonists**

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

### **Monoamine Oxidase Type B Inhibitors**

**B** - MAOB inhibitors should not be used as neuroprotective therapies for people with PD, except in the context of clinical trials.

## **Symptomatic Pharmacological Therapy in Parkinson's Disease**

### **Early Pharmacological Therapy**

#### *Levodopa*

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

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

#### *Dopamine Agonists*

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

**D (GPP)** - 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)** - 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.

(Full details of the restrictions on pergolide\* use and monitoring are available in the [Summary of Product Characteristics](#).)

**\*Note from the National Guideline Clearinghouse (NGC):** On March 29, 2007, Permax (pergolide) was withdrawn from the market in the U.S. and worldwide due to safety concerns of an increased risk of cardiovascular events. See the [U.S. Food and Drug Administration \(FDA\) Web site](#) for more information.

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

#### *Monoamine Oxidase Type B Inhibitors*

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

#### *Beta-Adrenergic Antagonists (Beta-Blockers)*

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

#### *Amantadine*

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

#### *Anticholinergics*

**B** - 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.

### **Comparisons of Drug Classes**

#### *Modified-Release Compared with Immediate-Release Levodopa*

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

### **Choice of Initial Pharmacological Therapy in Early Parkinson's Disease**

**D (GPP)** - 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

## Later Pharmacological Therapy

### *Levodopa*

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

### *Dopamine Agonists*

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

**D (GPP)** - 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. (Full details of the restrictions on pergolide\* use and monitoring are available in the [Summary of Product Characteristics](#).)

**\*Note from the National Guideline Clearinghouse (NGC):** On March 29, 2007, Permax (pergolide) was withdrawn from the market in the U.S. and worldwide due to safety concerns of an increased risk of cardiovascular events. See the [U.S. Food and Drug Administration \(FDA\) Web site](#) for more information.

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

### *Monoamine Oxidase Type B (MAOB) Inhibitors*

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

### *Catechol-O-Methyl Transferase Inhibitors*

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

**D (GPP)** - 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 (Trade name Stalevo® [Orion]).

**D (GPP)** - 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 therapy, and thereafter in accordance with the [Summary of Product Characteristics](#).

### *Amantadine*

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

### *Apomorphine*

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

**D** - 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.

### **Choice of Pharmacological Therapy in Later Parkinson's Disease**

**D (GPP)** - 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

**D (GPP)** - 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.

**D (GPP)** - 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.

**D (GPP)** - 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:

- 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

**D (GPP)** - 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.

### **Surgery for Parkinson's Disease**

#### **Subthalamic Nucleus (STN) Stimulation**

**D** - Bilateral STN 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

### **Globus Pallidus Interna (GPI) Stimulation**

**D (GPP)** - 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

### **Comparison of Different Types of Deep Brain Stimulation (DBS)**

**D (GPP)** - 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

### **Thalamic Stimulation**

**D** - 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.

### **Non-Motor Features of Parkinson's Disease**

#### **Mental Health Problems**

##### *Depression*

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

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

##### *Psychotic Symptoms*

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

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

**D (GPP)** - 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)** - 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)** - 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.

**B** - 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.

### *Dementia*

**D (GPP)** - 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.

### **Sleep Disturbance**

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

**D (GPP)** - 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, H<sub>2</sub> antagonists, antipsychotics and sedatives)

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

**D (GPP)** - 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.

#### *Daytime Hypersomnolence*

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

#### *Nocturnal Akinesia*

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

### **Falls**

#### *Assessment and Prevention of Falls*

**(NICE 2004)** - For all people with PD at risk of falling, please refer to the National Guideline Clearinghouse summary of the NICE guideline, [Clinical practice guideline for the assessment and prevention of falls in older people](#).

### **Autonomic Disturbance**

**D (GPP)** - People with PD should be treated appropriately for the following autonomic disturbances:

- Urinary dysfunction
- Weight loss
- Dysphagia
- Constipation
- Erectile dysfunction
- Orthostatic hypotension
- Excessive sweating
- Sialorrhoea

### **Other Key Interventions**

#### **Parkinson's Disease Nurse Specialist Interventions**

**C** - 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.

## **Physiotherapy**

**B** - 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

**C** - 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.

## **Occupational Therapy**

**D (GPP)** - 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

## **Speech and Language Therapy**

Speech and language therapy should be available for people with PD. Particular consideration should be given to:

- **B** - Improvement of vocal loudness and pitch range, including speech therapy programmes such as Lee Silverman Voice Treatment (LSVT)
- **D (GPP)** - 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 the safety and efficiency of swallowing and to minimise the risk of aspiration

## **Palliative Care in Parkinson's Disease**

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

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

## **Definitions:**

## Levels of Evidence for Intervention Studies

**1++** High quality meta-analysis (MA), systematic reviews (SR) of randomised controlled trials (RCTs), or RCTs with a very low risk of bias

**1+** Well conducted MA, SR or RCTs, or RCTs with a low risk of bias

**1-** MA, SR of RCTs, or RCTs with a high risk of bias

**2++** High quality SR 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-analytic studies (for example, case reports, case series)

**4** Expert opinion, formal consensus

## Levels of Evidence for Studies of the Accuracy of Diagnostic Tests

**Ia** Systematic review (with homogeneity)\* of level-1 studies\*\*

**Ib** Level-1 studies\*\*

**II** Level-2 studies\*\*\*  
Systematic reviews of level-2 studies

**III** Level-3 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'

\*Homogeneity means there are no or minor variations in the directions and degrees of results between individual studies that are included in the systematic review.

\*\*Level-1 studies are studies:

- That use a blind comparison of the test with a validated reference standard (gold standard)
- In a sample of patients that reflects the population to whom the test would apply.

\*\*\*Level-2 studies are studies that have **only one** of the following:

- Narrow population (the sample does not reflect the population to whom the test would apply)

- Use a poor reference standard (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
- Case-control studies

\*\*\*\*Level-3 studies are studies that have **at least two or three** of the features listed for level-2 studies.

## **Classification of Recommendations**

### **Grade A:**

- Level 1++ and directly applicable to the target population, or
- Level 1+ and directly applicable to the target population AND consistency of results
- Evidence from National Institute for Health and Clinical Excellence (NICE) technology appraisal

### **Grade B:**

- Level 2 ++, directly applicable to the target population and demonstrating overall consistency of results, or
- Extrapolated evidence from studies rated as 1++ or 1+

### **Grade C:**

- Level 2+, directly applicable to the target population and demonstrating overall consistency of results, or
- Extrapolated evidence from studies rated as 2++

### **Grade D:**

- Level 3 or 4, or
- Extrapolated from 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

## **Grading of Recommendations on Diagnostic Tests**

**Grade A (DS)** Studies with level of evidence Ia or Ib

**Grade B (DS)** Studies with level of evidence II

**Grade C (DS)** Studies with level of evidence III

**Grade D (DS)** Studies with level of evidence IV

(DS, diagnostic studies)

## CLINICAL ALGORITHM(S)

Clinical algorithms are provided in the original guideline document for:

- Parkinson's disease (PD)
- Management of psychosis in PD

## EVIDENCE SUPPORTING THE RECOMMENDATIONS

### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

- The use of the most appropriate modalities to diagnose Parkinson's disease (PD) enabling early diagnosis and avoiding unnecessary procedures for the patient
- The use of the most appropriate treatments to enable the best possible outcomes and minimum treatment-related adverse events for patients with PD

### POTENTIAL HARMS

- Levodopa preparations contribute to the development of motor complications in PD. These comprise abnormal involuntary movements or dyskinesias, such as athetosis and dystonia, along with response fluctuations in which people experience 'wearing off' of the drug's effects and/or unpredictable switching between the 'on' and the 'off' state.
- Ergot-derived dopamine agonists (bromocriptine, cabergoline, lisuride and pergolide\*) are well known to cause rare serosal reactions such as pleural, pericardial and peritoneal effusion and/or fibrosis

**\*Note from the National Guideline Clearinghouse (NGC):** On March 29, 2007, Permax (pergolide) was withdrawn from the market in the U.S. and worldwide due to safety concerns of an increased risk of cardiovascular events. See the [U.S. Food and Drug Administration \(FDA\) Web site](#) for more information.

- 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.

- Clozapine may be used in the treatment of psychotic symptoms in Parkinson's disease (PD), but registration with a mandatory monitoring scheme is required.
- Tolcapone has caused rare cases of fatal hepatic toxicity and neuroleptic malignant syndrome. As a result, it can only be used in England and Wales after a patient has failed on entacapone and its use requires intensive monitoring of hepatic function
- Amantadine has been reported to cause side effects including confusion, worsening of hallucinations, reappearance of palpitations, nausea, reversible oedema, dry mouth and constipation.
- Common events associated with intermittent subcutaneous apomorphine injections included: injection site complaints, drowsiness, yawning, dyskinesias, nausea or vomiting, chorea, sweating and warmth, dizziness, headache, rhinitis. Other events included: nausea, dyskinesia, short-lasting twinkling (sic) in legs, shortlasting worsening of tremor, warmth and sweating, lower level of motor functioning at end of clinical effect compared with basic level before the test.
- Apomorphine infusions have been associated with subcutaneous nodules. Other effects were: rhinorrhoea, nausea and hiccups, recurrent diarrhoea, confusion and emotional lability, euphoria and dysarthria, worsening of dyskinesia, orthostatic hypotension, psychosis, hallucinations, intermittent illusions, confusion, sleepiness, vertigo, eosinophilia, increased appetite, increased libido, visual delusions, diurnal agitation, immune haemolytic anaemia, mild self-limiting leg oedema, positive direct anti-globulin test without associated haematological changes.
- There is a small but significant risk of permanent neurological disability as a consequence of subthalamic nucleus stimulation and globus pallidus interna stimulation due mostly to cerebral infarction or haemorrhage. In a small number of patients, this can lead to death. Most other adverse effects of surgery were transient but concern remains regarding the incidence of neuropsychiatric complications, particularly depression and suicide. It is difficult to comment reliably on such issues in the absence of a control group.
- Thalamic stimulation carries a risk of serious complications such as cerebral infarction and haemorrhage.

## CONTRAINDICATIONS

### CONTRAINDICATIONS

Pergolide\* is contraindicated in anyone with anatomical evidence of cardiac valvulopathy.

**\*Note from the National Guideline Clearinghouse (NGC):** On March 29, 2007, Permax (pergolide) was withdrawn from the market in the U.S. and worldwide due to safety concerns of an increased risk of cardiovascular events. See the [U.S. Food and Drug Administration \(FDA\) Web site](#) for more information.

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

- Healthcare providers need to use clinical judgement, knowledge and expertise when deciding whether it is appropriate to apply guidelines. The recommendations cited here are a guide and may not be appropriate for use in all situations. The decision to adopt any of the recommendations cited here must be made by the practitioner in light of individual patient circumstances, the wishes of the patient, clinical expertise and resources.
- The National Collaborating Centre for Chronic Care (NCC-CC) disclaims any responsibility for damages arising out of the use or non-use of these guidelines and the literature used in support of these guidelines.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

#### Audit Criteria

The audit criteria shown in Table 3.1 of the original full-length guideline document are linked to the key priorities for implementation. These are intended to be suggestions to aid and monitor the implementation of this guideline at the level of a National Health Service (NHS) trust or similar scale healthcare provider.

### IMPLEMENTATION TOOLS

Audit Criteria/Indicators  
 Clinical Algorithm  
 Patient Resources  
 Quick Reference Guides/Physician Guides  
 Resources  
 Slide Presentation

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

End of Life Care  
 Living with Illness

### IOM DOMAIN

Effectiveness  
 Patient-centeredness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

National Collaborating Centre for Chronic Conditions. Parkinson's disease. National clinical guideline for diagnosis and management in primary and secondary care. London (UK): Royal College of Physicians; 2006. 237 p. [418 references]

## **ADAPTATION**

Not applicable: The guideline was not adapted from another source.

## **DATE RELEASED**

2006 Jun

## **GUIDELINE DEVELOPER(S)**

National Collaborating Centre for Chronic Conditions - National Government Agency [Non-U.S.]

## **SOURCE(S) OF FUNDING**

National Institute for Health and Clinical Excellence (NICE)

## **GUIDELINE COMMITTEE**

Guideline Development Group

## **COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE**

*Group Members:* Carl Clarke, Clinical Advisor, City Hospital and University of Birmingham, NCC-CC; Tara Sullivan, Research Fellow and Project Manager, NCC-CC; Alastair Mason, Chairman, NCC-CC; Bernadette Ford, Information Scientist, NCC-CC; Debbie Nicholl, Health Economist NCC-CC; Jill Parnham, Senior Research Fellow, NCC-CC; Nicole Wilson, Project Manager, NCC-CC (6 months); David Anderson, Consultant Psychiatrist, Mossley Hill Hospital, Liverpool, Royal College of Psychiatrists; Angela Birleson, Advanced Practitioner in Occupational Therapy, Occupational Therapy, Clinical Support Services, South Tees Hospitals NHS Trust, College of Occupational Therapists; David Burn, Consultant, Neurologist Newcastle General Hospital, Newcastle upon Tyne, Royal College of Physicians of London; Michael Godfrey, Patient Representative, Parkinson's Disease Society; Jacqui Handley, Parkinson's Disease Nurse Specialist, Dorset County Hospital, Dorchester, Parkinson's Disease Nurse Specialist Association; John Hindle, Consultant Physician, Care of the Elderly; North West Wales NHS Trust, Bangor; British Geriatrics Society; Brian Hurwitz, General Practitioner, King's College London, Royal College of General Practitioners; Andrew Lees, Professor of Neurology, Reta Lila Weston Institute of Neurological Studies, Institute of Neurology, University College London, Association of British Neurologists; Doug MacMahon, Consultant Physician with special responsibility for the elderly) Royal Cornwall Hospitals, NHS Trust Society, British Geriatrics; Robert Meadowcroft, Director of Policy, Campaigns and Information, Parkinson's Disease Society, Parkinson's Disease Society (Attended ten meetings); David McNiven, Policy and Campaigns Manager, Parkinson's Disease Society, Parkinson's Disease Society (Attended ten meetings); Bhanu Ramaswamy, Consultant Physiotherapist, Walton

Hospital, Chesterfield, Chartered Society of Physiotherapy; Julia Johnson (Expert advisor) Speech and Language Therapist, King's College Hospital London, Royal College of Speech and Language Therapists; TRK Varma (Expert advisor) Consultant Neurosurgeon, Walton Centre for Neurology & Neurosurgery, Liverpool, Society of British Neurological Surgeons; Ana Aragon (Deputy for Angela Birluson) Occupational Therapist, Bath and North East Somerset PCT, College of Occupational Therapists (Attended one meeting); Ira Leroi (Deputy for David Anderson) Consultant in Old Age Psychiatry, Manchester Mental Health and Social Care Trust, Royal College of Psychiatrists (Attended one meeting); Karen Durrant (Deputy for Bhanu Ramaswamy) Superintendent Physiotherapist, Walton Hospital, Chesterfield Chartered Society of Physiotherapy (Attended one meeting); David Stewart (Deputy for Doug MacMahon) Consultant Physician (medicine for the elderly), Mansionhouse Unit, Victoria Infirmary Glasgow, British Geriatrics Society (Attended one meeting)

## **FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST**

At each Guideline Development Group (GDG) meeting, all GDG members declared any potential conflict of interests.

## **GUIDELINE STATUS**

This is the current release of the guideline.

## **GUIDELINE AVAILABILITY**

Electronic copies: Available from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).

## **AVAILABILITY OF COMPANION DOCUMENTS**

The following are available:

- Diagnosis and management in primary and secondary care. London (UK): National Institute for Health and Clinical Excellence; 2006 Jun. 45 p. (Clinical guideline; no. 35). Electronic copies: Available in Portable Document Format (PDF) from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).
- Diagnosis and management in primary and secondary care. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence; 2006 Jun. 15 p. (Clinical guideline; no. 35). Electronic copies: Available in Portable Document Format (PDF) from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).
- Parkinson's disease: diagnosis and management in primary and secondary care. National cost-impact report. London (UK): National Institute for Health and Clinical Excellence; 2006 Jun. 31 p. (Clinical guideline; no. 35). Electronic copies: Available in Portable Document Format (PDF) from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).
- Costing impact of the NICE guideline on Parkinson's disease – England. London (UK): National Institute for Health and Clinical Excellence; 2006 Jun. various p. (Clinical guideline; no. 35). Electronic copies: Available in Portable

Document Format (PDF) from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).

- Implementation advice. Parkinson's disease. London (UK): National Institute for Health and Clinical Excellence; 2006 Jun. 19 p. (Clinical guideline; no. 35). Electronic copies: Available in Portable Document Format (PDF) from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).
- Parkinson's disease. Presenter's slides. London (UK): National Institute for Health and Clinical Excellence; 2006 Jun. 24 p. (Clinical guideline; no. 35). Electronic copies: Available in Portable Document Format (PDF) from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).
- Guidelines manual 2006. London (UK): National Institute for Health and Clinical Excellence; 2006 Feb. Electronic copies: Available in Portable Document Format (PDF) from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N1052. 11 Strand, London, WC2N 5HR.

Additionally, audit criteria are provided in Table 3.1 of the [original guideline document](#).

## **PATIENT RESOURCES**

The following is available:

- Parkinson's disease. Understanding NICE guidance. Information for people who use NHS services. National Institute for Clinical Excellence (NICE), 2006 Jun. 15 p. Available in Portable Document Format (PDF) from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455, ref: N1053. 11 Strand, London, WC2N 5HR.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

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