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An assessment of the relative cost-effectiveness of different classes of drugs for Parkinson's disease

Submission date
25/04/2003

Recruitment status
No longer recruiting

Registration date
25/04/2003

Overall study status
Completed

Last Edited
30/12/2021

Condition category
Nervous System Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Parkinson's disease (PD) is a movement disorder that causes stiffness in the muscles, slowness and tremor. These symptoms appear over many years and are caused by a reduction in the numbers of brain cells that produce a chemical called dopamine. Several different types of drugs (mainly levodopa, dopamine agonists, MAOB inhibitors and COMT inhibitors) are used to control the symptoms of PD, with some doctors preferring one type and other doctors another. However, little is known about how the drugs compare with each other and whether or not some provide better overall quality of life for people with PD. The aim of this study is to compare the different drugs for PD to find out which treatment achieves the best control of symptoms with the fewest side-effects.

Who can participate?
Recently diagnosed patients with PD and patients with poorly controlled PD

What does the study involve?
Participants are randomly allocated to be treated with one of the different types of drug. These are prescribed by their doctor in the usual way and the participants are asked to complete questionnaires every year for at least 5 years to say how the drugs are affecting them. The participants' carers are also asked how helping to look after someone with PD affects their life. The questionnaires are sent out by post and no extra clinic visits are necessary.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
University of Birmingham Clinical Trials Unit

When is the study starting and how long is it expected to run for?
November 1999 to October 2011

Who is funding the study?
Health Technology Assessment Programme (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2005-001813-16

Protocol serial number
HTA 98/03/02; Protocol Version 7.1

Study information

Scientific Title
A large randomised assessment of the relative cost-effectiveness of different classes of drugs for Parkinson's disease

Acronym
PD MED

Study objectives
Clinical trials comparing different classes of Parkinson's disease drugs have been too small for reliable conclusions, have used inappropriate surrogate endpoints, and follow-up has been too short to evaluate long-term benefits and toxicity. This large (5000 patients), pragmatic, 'real-life' randomised trial addresses four fundamental, unanswered questions about PD treatment: what are the costs and benefits of:

1. Levodopa [LD]-sparing therapy (dopamine agonist [DA] or monoamine oxidase type B [MAOB] inhibitors) compared to LD alone in initial treatment
2. DAs compared to MAOB inhibitors as initial LD-sparing therapy
3. DAs compared to dopamine degradation inhibitors [DDIs] (catechol-O-methyltransferase [COMT] or MAOB inhibitors) when motor fluctuations develop on LD alone
4. COMT inhibitors compared to MAOB inhibitors as DDI in advanced disease.

Two separate three-way randomisations allow classes of treatments for early and advanced disease to be investigated. Secondary objectives are to identify factors that might predict response to particular classes of drug and to provide a large collaborative framework within which other studies - in particular of neurosurgery and genetics - can be undertaken.

More details can be found at: http://www.nets.nihr.ac.uk/projects/hta/980302
Protocol can be found at: http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0012/54120/PRO-98-03-02.pdf

Ethics approval required
Old ethics approval format

Ethics approval(s)
West Midlands REC, 27/04/2000, ref: MREC00/7/17

Study design
Randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Parkinson's disease

Interventions
Current interventions as of 05/05/2009:

Early PD randomisation
Patients with early PD are randomised between DA (+/- LD), MAOBI (+/- LD) and LD alone, with the option to omit either the MAOBI or LD alone arm. If treatment with either MAOBI or LD alone is considered to be definitely inappropriate for a particular patient, then this arm can be omitted.

Later PD randomisation
Those whose disease is no longer controlled by their first class of drug, after dose titration and /or addition of LD, are randomised between COMTI (+/- LD), MAOBI (+/- LD) and DA (+/- LD), with the option to omit either the MAOBI or the DA arm. Patients who were already receiving a DA when uncontrolled motor complications arose are not eligible for the DA arm but can be randomised between COMTI and MAOBI. Patients who were receiving a MAOBI when

uncontrolled motor complications arose, or for whom the clinician considers that MAOBI treatment is definitely contraindicated, are not eligible for the MAOBI arm but can be randomised between COMTI and DA.

N.B. Patients who have been entered into the early disease randomisation should be re-randomised into the later disease randomisation if motor complications develop that cannot be controlled by drug dose titration and/or addition of LD if on DA/MAOBI.

Dosage
The pragmatic 'real life' design of the trial allows clinicians to choose which DA, MAOBI and COMTI to use, and to vary the dose as they see fit. The eventual results will be more clinically relevant, in that drug usage will reflect normal clinical practice which involves frequent dose adjustments to achieve optimal symptom control.

Open label treatment
Blinding of treatment allocation is not considered necessary in PD MED because the potential for subjectively biased assessment is small. There is no reason to expect that patients will have any prior beliefs that one treatment will be better than another (all patients in both randomisations receive active therapy - there are no placebo arms).

The duration of interventions will vary between individual participants. All participants will be followed up for at least 10 years (unless they die or withdraw from the trial).

Previous interventions:
New vs old drugs for PD

Intervention Type
Drug

Phase
Not Applicable

Primary outcome(s)
Current primary outcome measures as of 21/04/2009:
1. Patient's self-evaluation of their functional status and quality of life (using the Parkinson's Disease Questionnaire 39 [PDQ-39])
2. Cost-effectiveness (EuroQoL EQ-5D)

All primary outcome measures will be assessed at baseline, 6 months and then at 1, 2, 3, 4 and 5 years.

Previous primary outcome measures:
PDQ-39 and EuroQol EQ-5D (Activities of Daily Living and Quality of life), caregiver wellbeing, time to treatment failure, long-term toxicity, formal and informal care costs. A cost-minimisation (if no clinical difference) or cost-utility (cost/QALY) analysis will be undertaken.

Key secondary outcome(s))
Added as of 21/04/2009:
1. Cognitive function (Mini Mental State Examination [MMSE]), assessed at baseline and 5 years
2. Wellbeing of carers (SF-36® Health Survey), assessed at baseline, 6 months and then at 1, 2, 3, 4 and 5 years

3. Resource usage, followed-up for 5 years
4. Toxicity and side-effects, including mortality rates, followed-up for 5 years
5. Time to onset of motor complications (early disease randomisation only) and time to surgical intervention or start of apomorphine (later disease randomisation only), followed-up for 5 years

Completion date
31/10/2011

Eligibility

Key inclusion criteria
Current inclusion criteria as of 21/04/2009:

Patients are eligible for the early disease randomisation if:
1. They are newly or recently diagnosed with Parkinson's disease. It is important to ensure the accurate diagnosis of PD and the UK Brain Bank criteria should be used
2. They have functional disability requiring medical therapy. Patients not thought to require dopaminergic treatment at diagnosis may be entered once it is considered that such treatment becomes necessary
3. They are previously untreated for PD or have been treated with dopaminergic PD medication for less than 6 months
4. There is no definite contraindication to, or definite indication for, any of the therapies to which they might be allocated (If it is considered that LD only is not an appropriate option for a patient, they may be randomised two ways between DA and MAOBI. Similarly, if a MAOBI is not considered appropriate, a patient may be randomised two ways between LD and DA.)
5. They are able to complete the trial questionnaires. Non-English-speaking patients may be entered if they have a carer, relative or other person who can help them fill in the questionnaires, or if translated documentation is available

Patients are eligible for the later disease randomisation if:
1. They have PD and develop motor complications that are uncontrolled by LD (either alone or in combination with either a DA or a MAOBI) and hence require the addition of another class of drug
2. There is no definite contraindication to, or definite indication for, any of the therapies to which they might be allocated. (Patients who were already receiving a DA when uncontrolled motor fluctuations arose are not eligible for the DA arm and will be randomised between MAOBI and COMTI only. Patients who were receiving a MAOBI when uncontrolled motor fluctuations arose, or for whom the clinician does not wish a MAOBI to be an option, are not eligible for the MAOBI arm and will be randomised between DA and COMTI only.)
3. They are able to complete the trial questionnaires. Non-English-speaking patients may be entered if they have a carer, relative or other person who can help them fill in the questionnaires, or if translated documentation is available.

Previous inclusion criteria:
Recently diagnosed patients with PD and patients with poorly controlled PD

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Senior

Sex
All

Key exclusion criteria
Added as of 21/04/2009:
Patients are not eligible for the early disease randomisation if:
1. They have received previous dopaminergic drug therapy for PD for more than 6 months
2. They are demented (as defined by the medical team responsible)
3. They are unable to give informed consent

Patients are not eligible for the later disease randomisation if:
1. They are demented (as defined by the medical team responsible)
2. They are unable to give informed consent

Date of first enrolment
01/11/1999

Date of final enrolment
31/10/2011

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Birmingham Clinical Trials Unit
Birmingham
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Sponsor information

Organisation
University of Birmingham (UK)

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Not provided at registration

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	27/09/2014		Yes	No
Results article	Long-term follow-up	28/12/2021	30/12/2021	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes