

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

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Registration date 25/04/2003	Overall study status Completed	<input type="checkbox"/> Protocol
Last Edited 30/12/2021	Condition category Nervous System Diseases	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> 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?
Prof. Richard Gray
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Study website
<http://www.pdmed.bham.ac.uk/>

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2005-001813-16

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
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

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

Patient information sheet can be found at: <http://www.birmingham.ac.uk/research/activity/mds/trials/bctu/trials/pd/pdmed/participants/sheets.aspx>

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 measure

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.

Secondary outcome measures

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

Overall study start date

01/11/1999

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

Age group

Senior

Sex

Both

Target number of participants

1500-2250 (1000-1500 and 500-750 in early and later disease, respectively)

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

England

United Kingdom

Study participating centre

University of Birmingham Clinical Trials Unit
Birmingham
United Kingdom
B15 2TT

Sponsor information

Organisation

University of Birmingham (UK)

Sponsor details

Edgbaston
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Sponsor type

University/education

Website

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ROR

<https://ror.org/03angcq70>

Funder(s)

Funder type

Government

Funder Name

Health Technology Assessment Programme

Alternative Name(s)

NIHR Health Technology Assessment Programme, HTA

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Results and Publications

Publication and dissemination plan

Not provided at time of registration

Intention to publish date

01/09/2017

Individual participant data (IPD) sharing plan

Not provided at registration

IPD sharing plan summary

Not provided at time of registration

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