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Current medical and
surgical treatment of
Parkinson's Disease

B

Professor Carl E Clarke
June 2011

NICE guidelines – June 2006

Key priorities for implementation

- **Referral to expert for accurate diagnosis**
 - **People with suspected PD should be referred quickly and untreated to a specialist with expertise in the differential diagnosis of this condition**
- **Expert review of diagnosis**
 - **The diagnosis of PD should be kept under regular review and re-considered if atypical clinical features develop**

U Diagnostic issues B

What else looks like PD?

□ Tremor

- Essential tremor

□ Parkinsonism

- Idiopathic Parkinson's disease
- Multiple infarct state - strokes
- Drug-induced - neuroleptics
- Trauma – pugilistic encephalopathy
- Toxin-induced - MPTP, CO, Mn, Cu
- Parkinson's plus syndromes

- Progressive Supranuclear Palsy

- Multiple System Atrophy

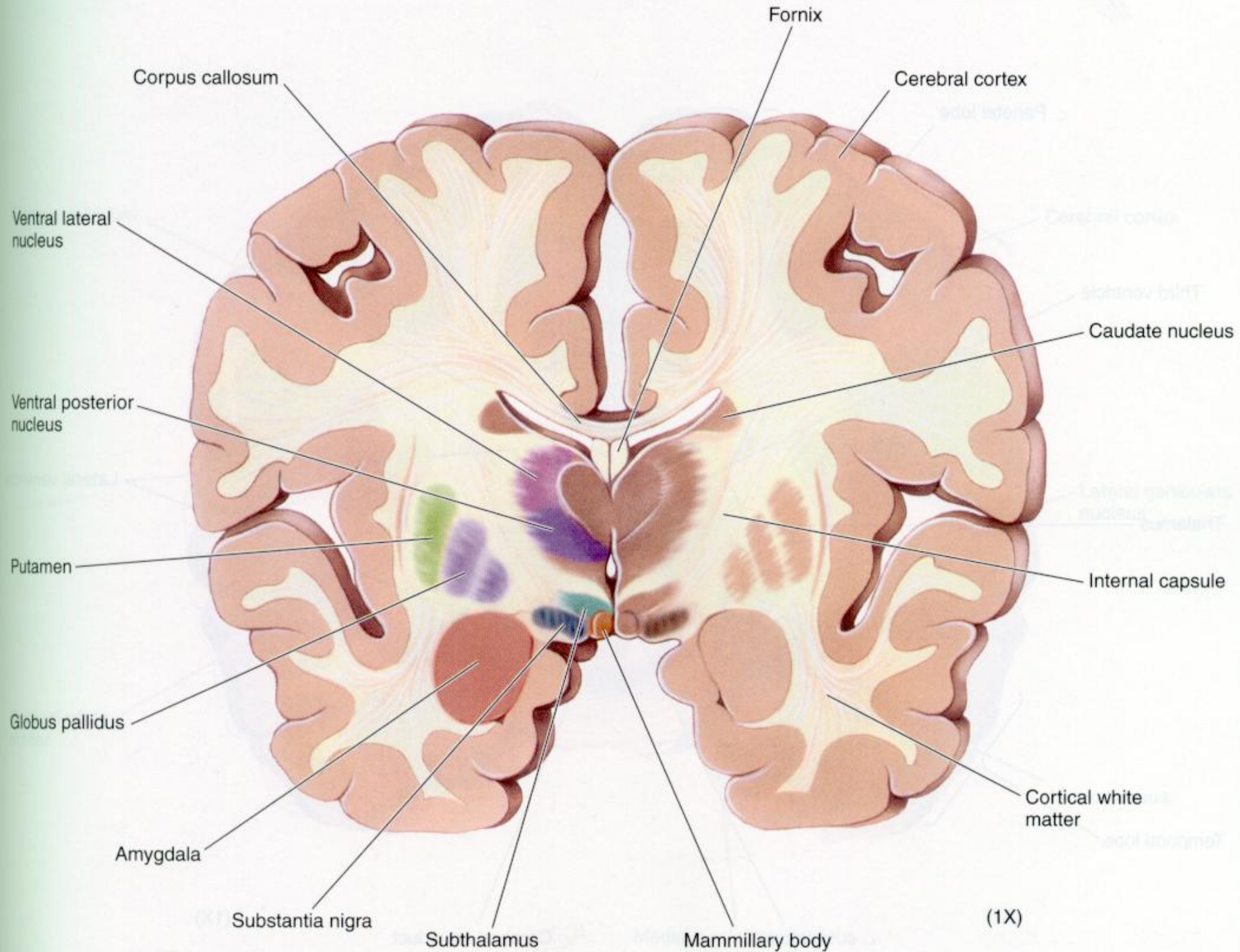
Idiopathic Parkinson's disease



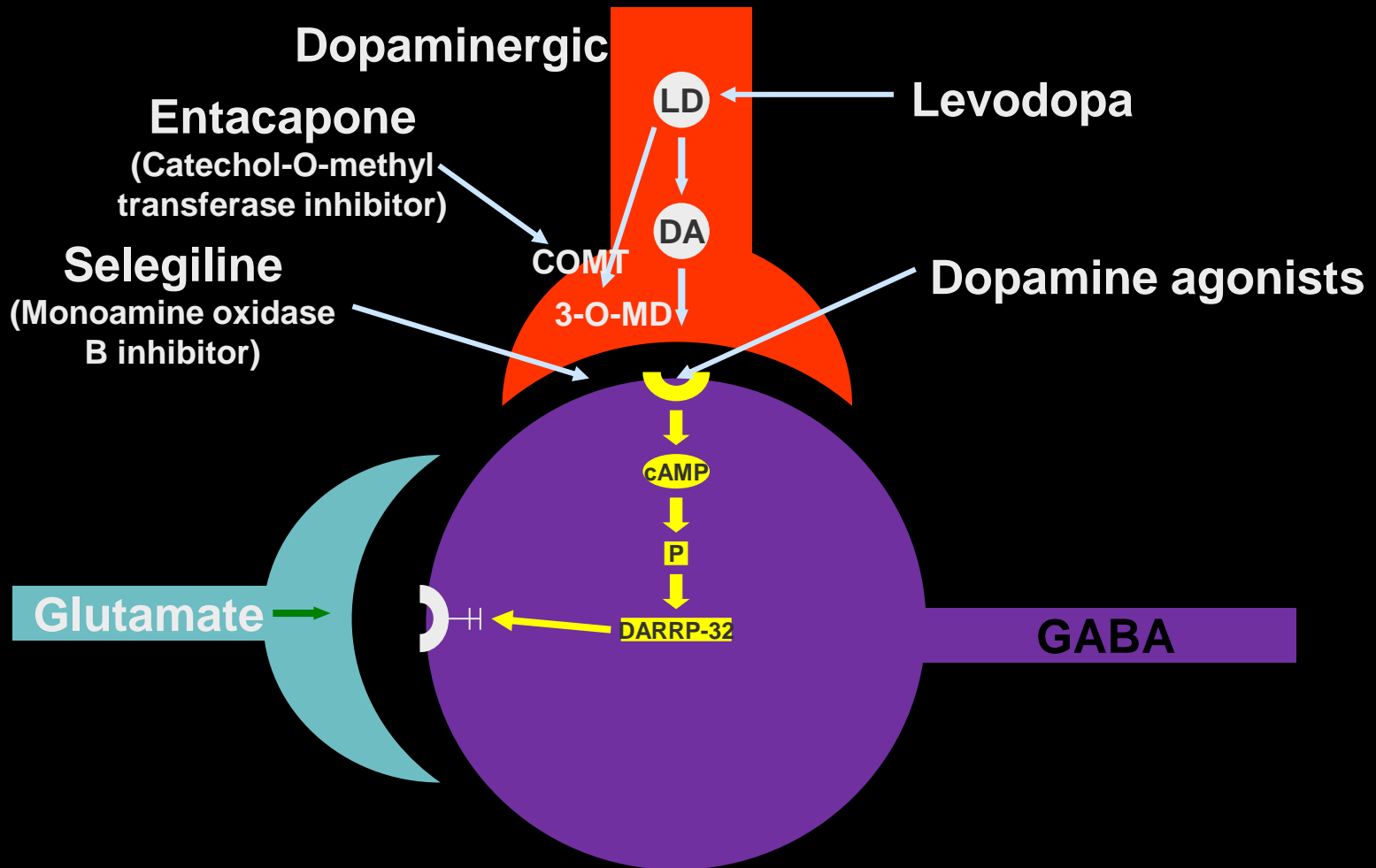
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Treatment issues

B



Drug classes in PD



NICE guidelines

Early disease options

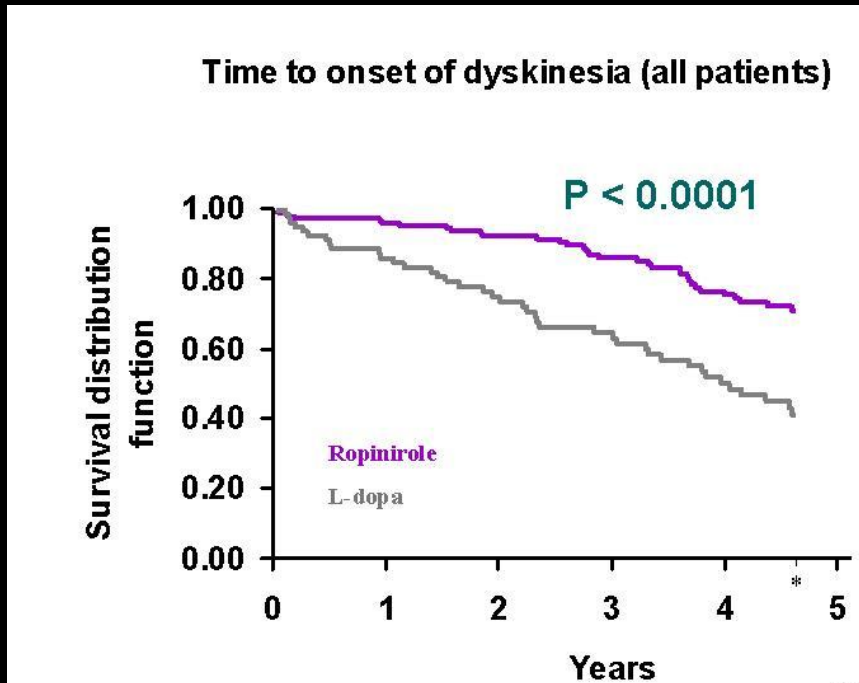
Initial therapy for early PD	First-choice option	Symptom control	Risk of side effects	
			Motor complications	Other adverse events
Levodopa	✓	+++	↑	↑
Dopamine agonists	✓	++	↓	↑
MAOB inhibitors	✓	+	↓	↑
Anticholinergics	✗	Lack of evidence	Lack of evidence	Lack of evidence
Beta-blockers	✗	Lack of evidence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

Motor complications

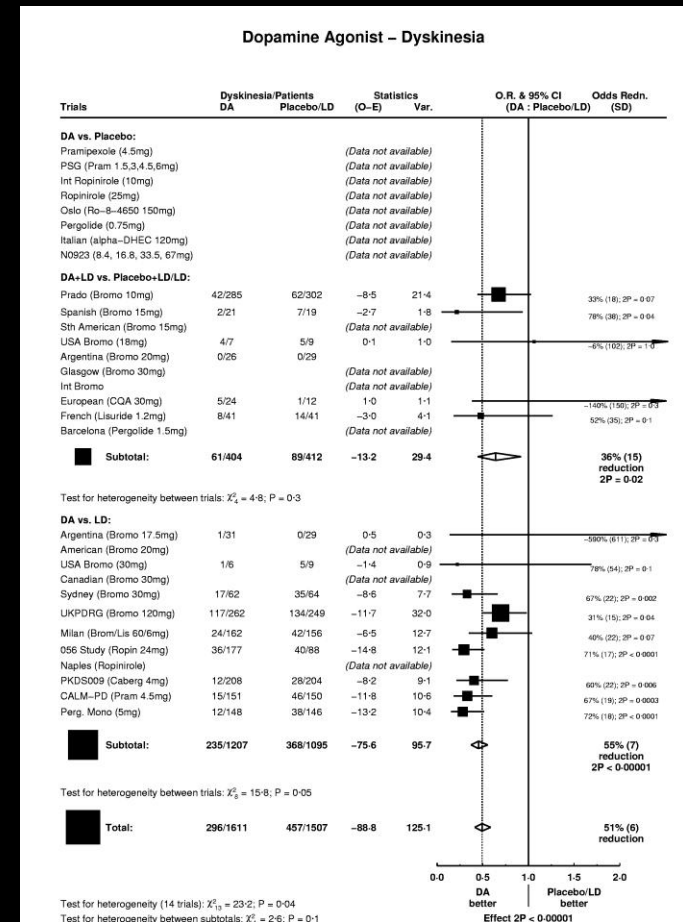


Dopamine agonists

Delay onset of motor complications



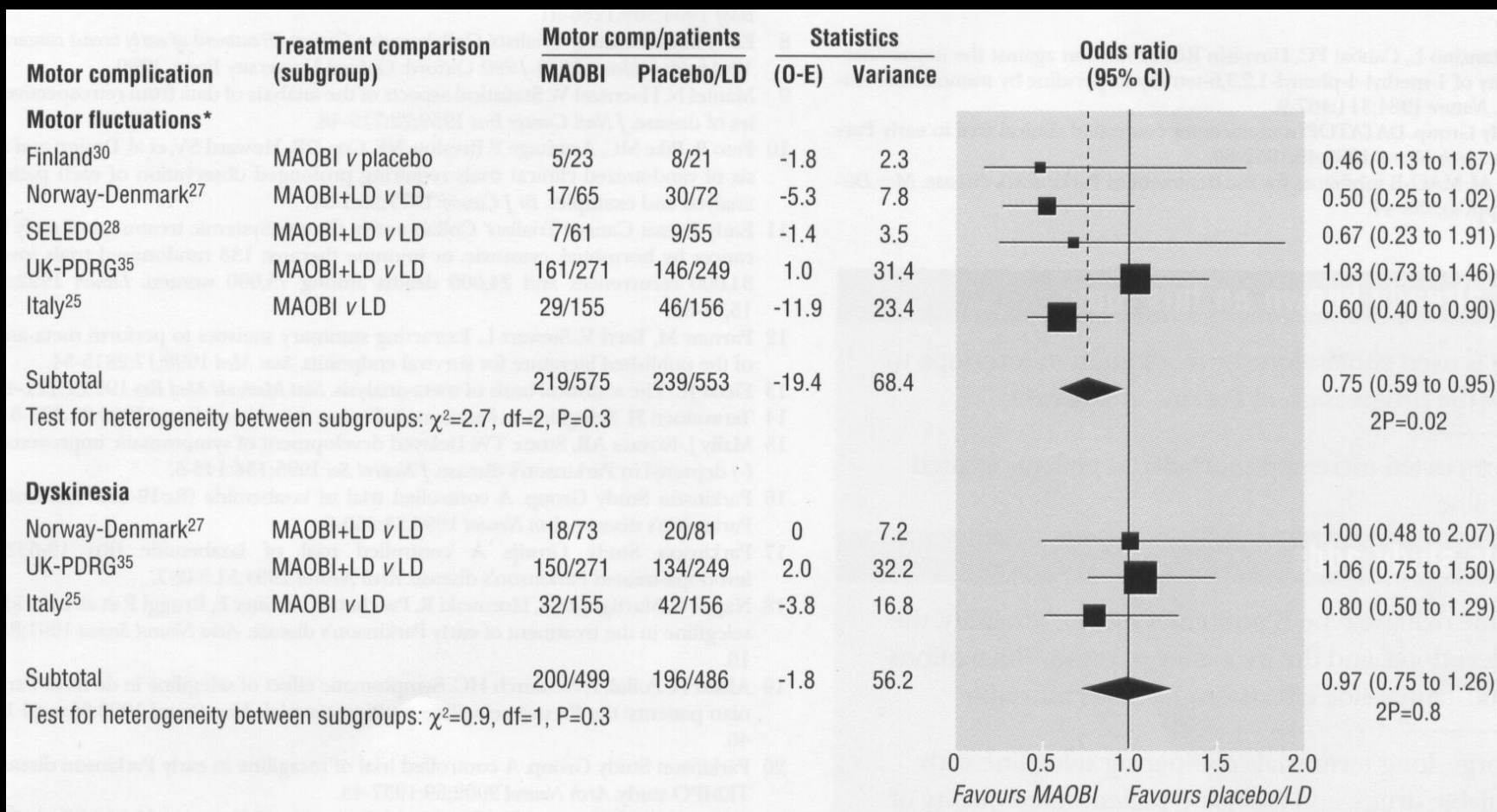
N Eng J Med 2000; 342: 1484-1491



Cochrane Database SR 2008

Monoamine oxidase B inhibitors

Delay onset of motor complications





PD MED Trial

Early disease randomisation



- **Large pragmatic randomised controlled trial:**
 - Levodopa
 - Dopamine agonist
 - MAOB inhibitor
- **Primary outcome measures**
 - Patient rated quality of life (PDQ 39 motor score)
 - Health economics
- **Recruitment ended Dec 2009 with n=1620**
- **First report Autumn 2011**

NICE guidelines

Later disease

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

Adjuvant placebo-controlled trials meta-analysis

- Dopamine agonists and tolcapone *superior* to entacapone and rasagiline in:
 - Reducing off time
 - Reducing levodopa dose
 - Without disproportionately increasing dyskinesia and dopaminergic adverse events



PD MED Trial

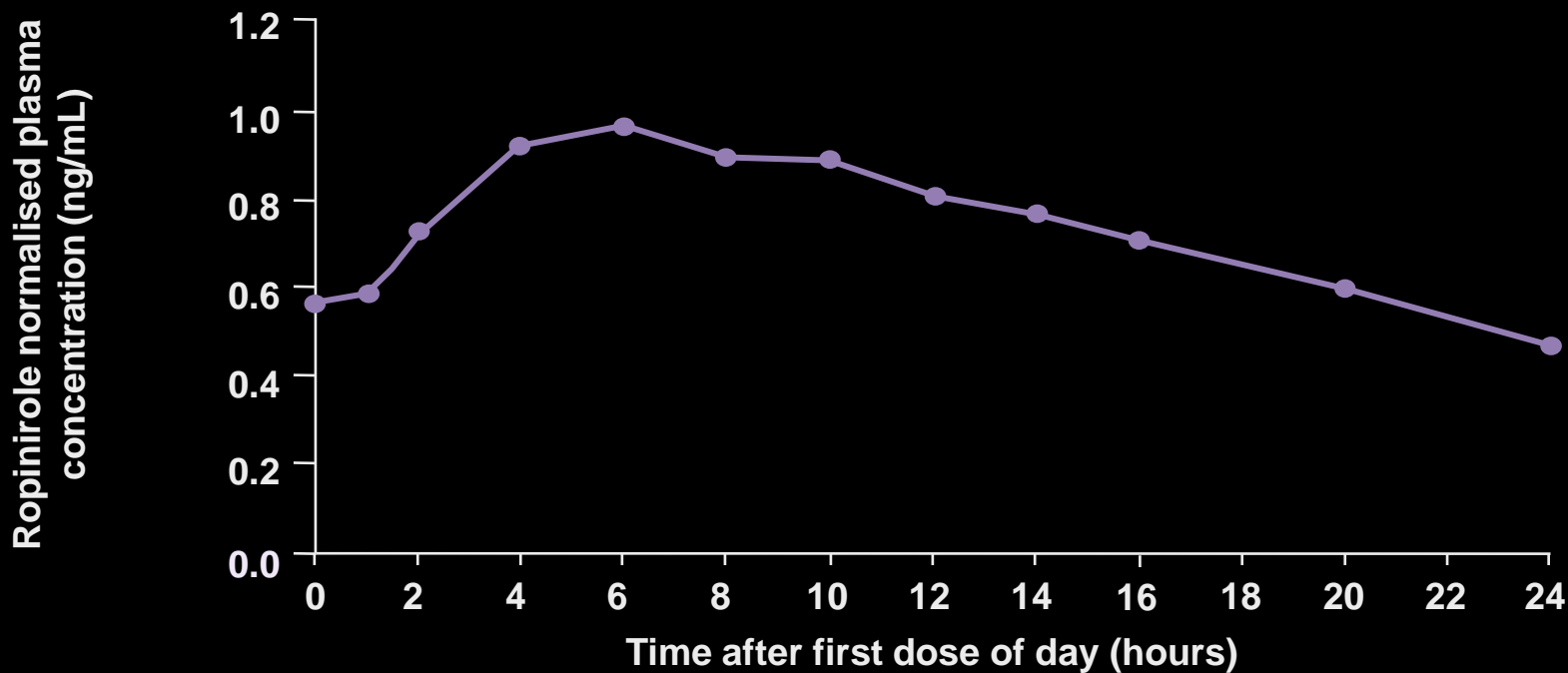
Later disease randomisation



- **Large pragmatic randomised controlled trial:**
 - Dopamine agonist
 - MAOB inhibitor
 - COMT inhibitor
- **Primary outcome measures**
 - Patient rated quality of life (PDQ 39 motor score)
 - Health economics
- **Recruitment ended Dec 2009 with n=500**
- **First report Autumn 2011**

Continuous dopaminergic stimulation with dopamine agonists

Prolonged-release ropinirole



Clin Ther. 2007; 29(12): 2654-66

Continuous dopaminergic stimulation with dopamine agonists

- **When/how to use:**
 - **Poor compliance**
 - **Nocturnal akinesia/dystonia**
 - **Early morning akinesia**
 - **(Reduce motor complications)**
 - **(Prevent motor complications)**
- **Care switching patient already on maximum dose of immediate-release dopamine agonist**
- **Cost issue**

Amantadine

- ❑ Old antiviral agent found to be effective in PD by chance
- ❑ Abandoned after 1970s in favour of agonists
- ❑ Found to have anti-dyskinetic effect in 4 RCTs in only 93 patients
- ❑ One RCT suggested effect only lasts 8 months
- ❑ 100 mg/d titrated up weekly by 100 mg to 100 mg tds

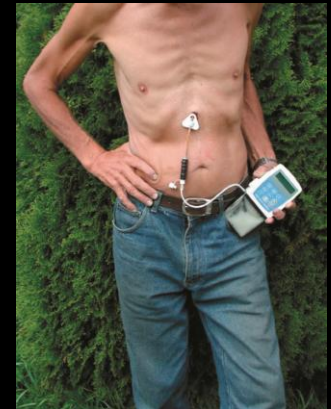
Severe motor disability

What then?

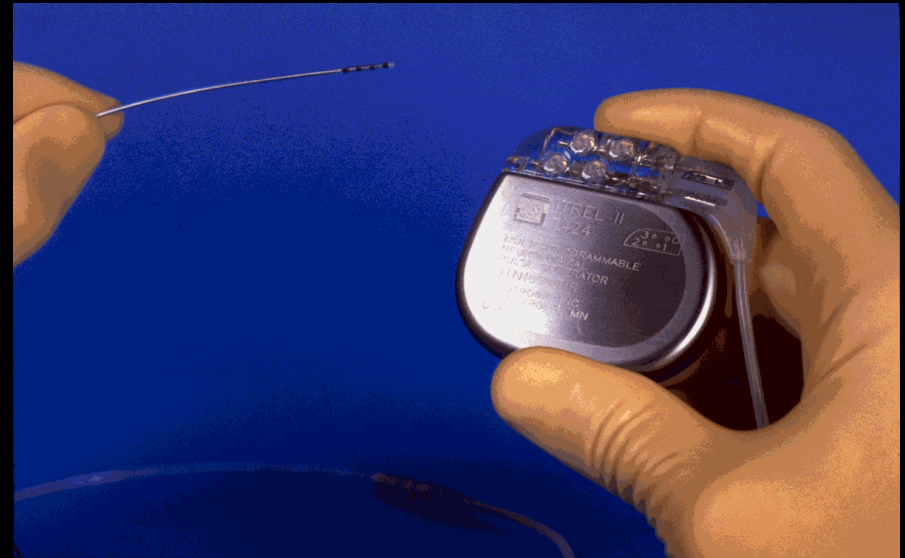
□ Subcutaneous apomorphine injections and infusions



□ Intrajejunal levodopa gel infusions (Duodopa®)



Subthalamic 'deep brain' stimulation





PD SURG



- UK PD SURG Trial
- RCT of STN DBS v delay surgery to end of waiting list (~12 months)
- Closed recruitment 31-12-06
- N = 366
- Baseline to 12 month change:
 - PDQ 39 Summary Index = -5.4 v +0.3 (p=0.0003)
 - PDQ 39 Mobility = -8.9 v +0.9 (p=0.002)
 - PDQ 39 ADL = -12.2 v +0.4 (<0.0001)

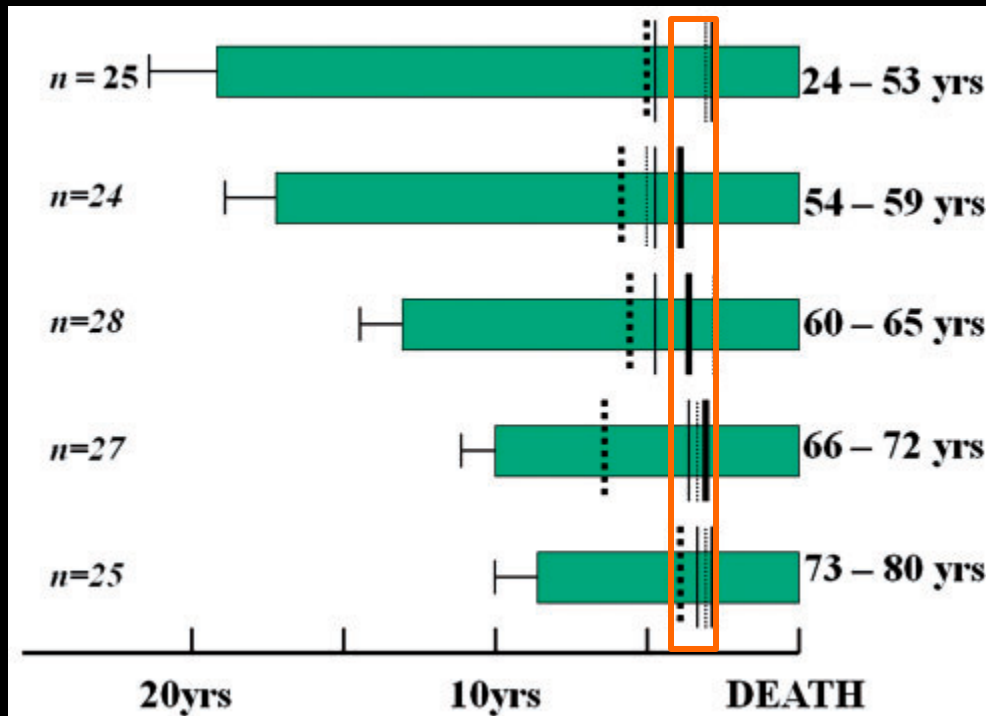
'Rational polypharmacy' in PD

- Levodopa or non-ergot dopamine agonist
- **Restrict levodopa dose - max. of ~ 600 mg/d**
- Add LD or DA as disease progresses
- Add entacapone for wearing off (as Stalevo®)
- If fails, try tolcapone
- Add rasagiline
- Add amantadine (for dyskinesia and wearing off)
- Add intermittent sc apomorphine
- Consider continuous apomorphine infusion
- Consider surgery
- Consider Duodopa®

Non-motor features of PD

- **Mental health**
 - **Dementia, depression, psychosis**
- **Falls**
- **Autonomic**
 - **Constipation, orthostatic hypotension, dysphagia**
- **Sleep disturbance**
 - **RBD, nocturnal akinesia & dystonia, RLS**
- **Pain**
 - **Frozen shoulder, co-morbid arthropathy**

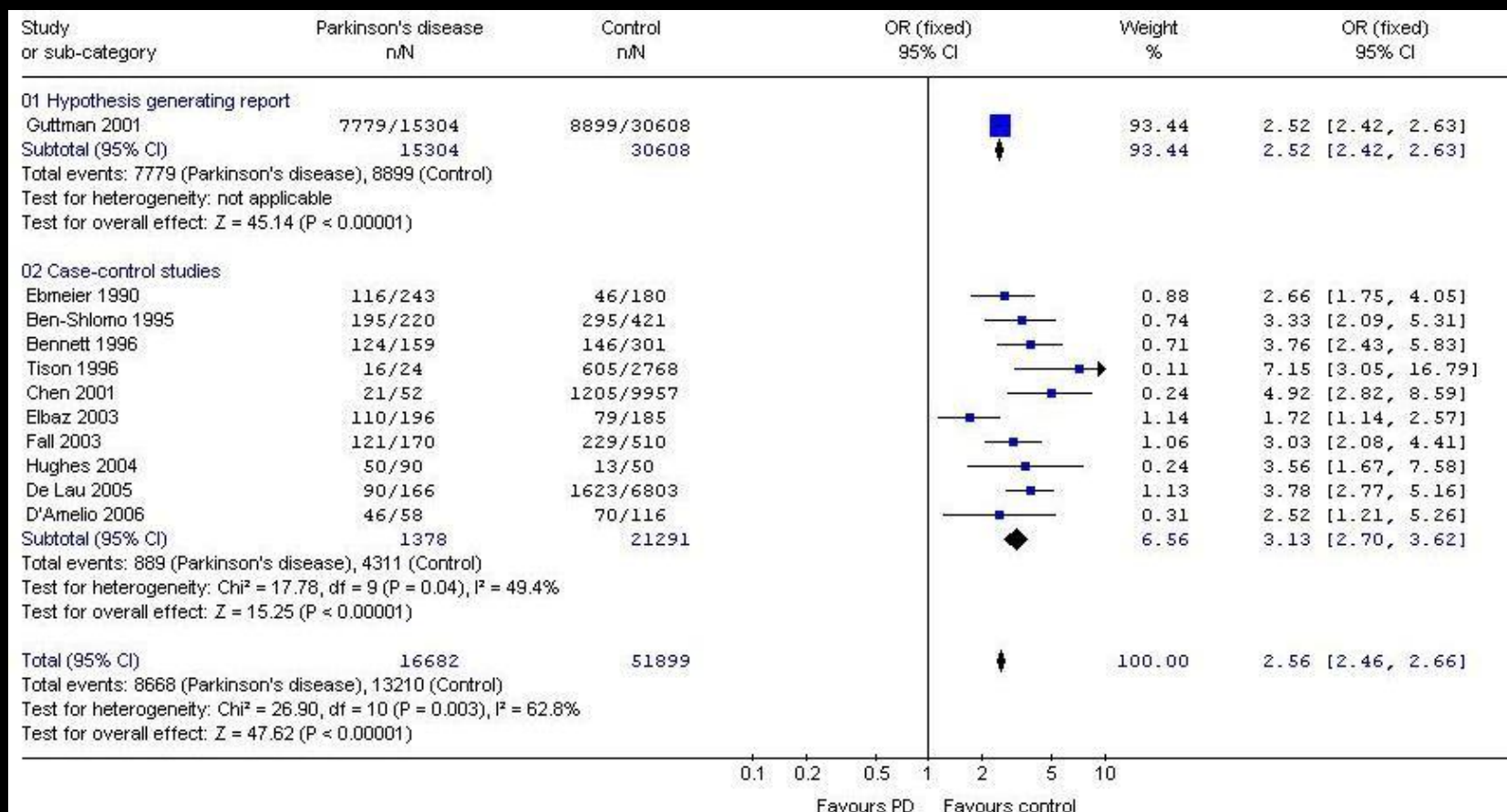
End of life issues



- Brain Bank cases
- Retrospective notes review
- Age at onset bands

Visual hallucinations = heavy dots
Regular falls = fine lines
Cognitive disability = fine dots
Residential care = heavy lines

End of life issues



J Neurol 2010; 257 (suppl 2):S262

**UNIVERSITY OF
BIRMINGHAM**

U Future

B

New drug classes in PD

