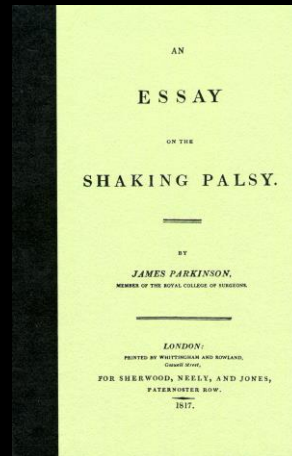


# As the going gets tough



Richard J Davenport  
Edinburgh

# Disclosures

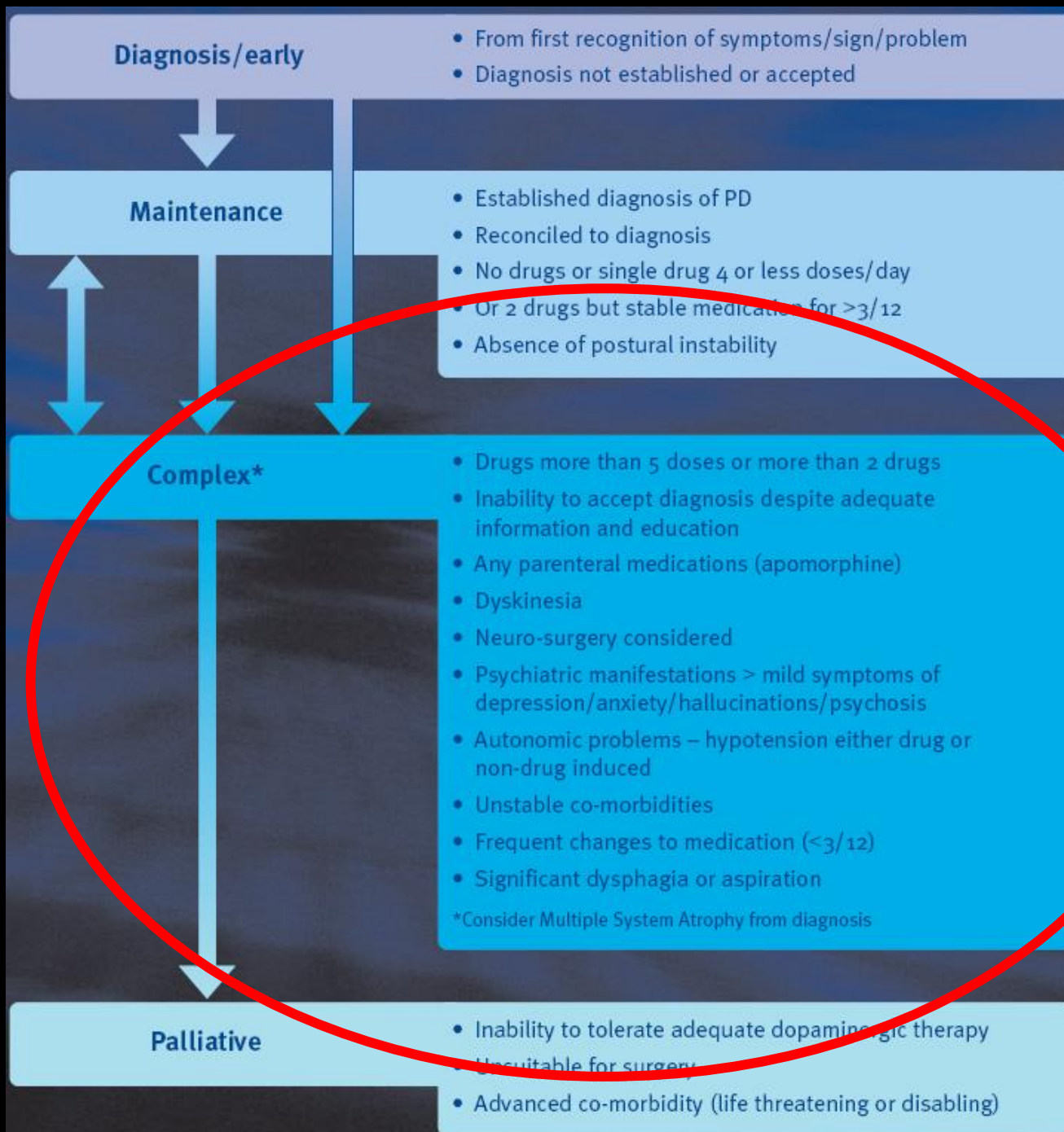
- Financial disclosures
  - UCB, Teva/Lundbeck, GSK, Genus/Britannia etc
- SIGN group (113) 2010
- Chair NACNC
- All slides are mine

# Viewer discretion



# When the going gets tough?

- What do we call this stage of PD?
  - Complex?
  - Progressive?
  - Advanced?
  - Difficult?
  - Late stage?
  - (Palliative)?



# As the years pass after diagnosis.....

- QoL ↑ affected by
  - Motor evolution
  - Non-motor symptoms
  - Other co-morbidities
- The consultation art
  - The good doctor/nurse/other
  - Inclusive, sensitive, aware, sympathetic/empathetic etc.....

# What happens to PD patients?

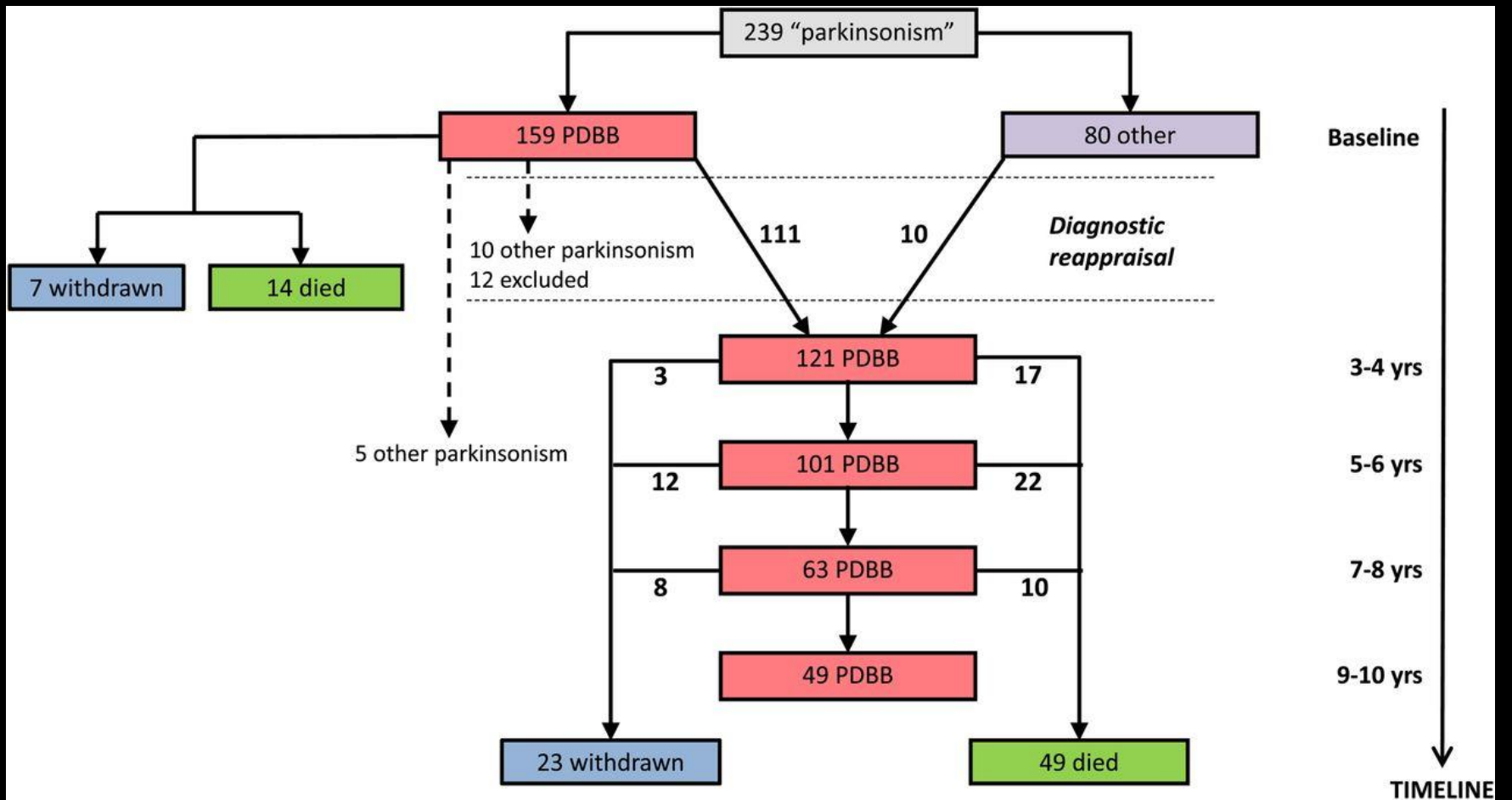
RESEARCH PAPER

## The CamPaIGN study of Parkinson's disease: 10-year outlook in an incident population-based cohort

Caroline H Williams-Gray,<sup>1</sup> Sarah L Mason,<sup>1</sup> Jonathan R Evans,<sup>1</sup> Thomas Foltynie,<sup>2</sup> Carol Brayne,<sup>3</sup> Trevor W Robbins,<sup>4</sup> Roger A Barker<sup>1</sup>

**To cite:** Williams-Gray CH, Mason SL, Evans JR, *et al.* *J Neurol Neurosurg Psychiatry* Published Online First: [please include Day Month Year] doi:10.1136/jnnp-2013-305277

- 2 year, prospective, community based incident cohort, treated
- 10 year follow up
- Mean age onset 70





# Outcome?

- N = 142
- At 10 years
  - 55% dead
  - 68% postural instability (PI)
  - 46% demented
  - 23% had “good” outcome
    - not dead/demented/falling

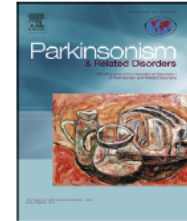


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Contents lists available at [ScienceDirect](#)

## Parkinsonism and Related Disorders

journal homepage: [www.elsevier.com/locate/parkreldis](http://www.elsevier.com/locate/parkreldis)



### Medium-term prognosis of an incident cohort of parkinsonian patients compared to controls

S. Fielding, A.D. Macleod, C.E. Counsell\*

*Institute of Applied Health Sciences, University of Aberdeen, Polwarth Building, Foresterhill, Aberdeen AB25 2ZD, UK*



- N=199 mean age diagnosis 75
- Median survival 7.8 yrs (<3 other parks)
- At 3 years dead/dependent
  - Controls: 21%
  - PD: 46%
  - Atypicals: 96%

# Motor fluctuations

- Wearing off
  - delayed ON
  - dose failures
- Dyskinesias
  - Peak dose or biphasic
  - Off dyskinesia (usually dystonia)
- ON/OFF fluctuations
- (Freezing and PI)

# Do people become “immune” to LD?

- No, but....
  - Complex interaction between PD and LD
  - Dyskinesias are LD related
  - Fluctuation encouraged by LD
  - Lots of PD symptoms never respond to LD
    - Tremor
    - Falling
    - Many non-motor symptoms

# What else happens?

- Non-motor symptoms
  - Neuropsychiatric
    - Anxiety/depression/apathy
    - Impulse control
    - Dopamine dysregulation
    - Hallucinosi/psychosis/paranoia
    - Cognitive impairment (dementia)
  - Pain
  - Sexual dysfunction
  - Drooling
  - Sphincter disturbance/constipation
  - Excessive sleepiness/insomnia/poor quality sleep
  - Etc.....
- Other pathology
- ...and get older

# Complex PD

- Characterised by
  - Onset of troublesome motor fluctuations
  - Postural instability
  - Cognitive decline
  - Progressive NMS
  - Increasing “resistance” to LD
  - ↓QoL (all)

# How to sort it (!)

- Problem list
  - Identify most significant
  - Multiple ascertainment
  - Don't restrict to PD or motor symptoms
- Decide
  - Can the problems be helped?
  - If so by whom and how?
  - Team approach

# Phone a friend

- Primary care
- PDNS
- Therapists
- Geriatrician
- Psychiatrist/MH teams
- Orthopaedics/rheumatology/eyes etc...



# The discussion

- Hard work
  - Tempting to skip
  - Be honest (limitations)
  - Neuromythology
  - No one knows all the answers
  - Palliative?

# The (ideal) discussion

- Identify and agree on problems
- Identify refractory symptoms
- Discuss options for more treatable
- Provide information
- Allow time to think

# Refractory symptoms

- Motor
  - Tremor (often)
  - Postural instability/falls
  - Speech
  - Freezing of gait
- NMS
  - Fatigue/apathy
  - Cognitive (?)
  - Pain
  - EDS etc....

# When the going gets tough: how to select patients with Parkinson's disease for advanced therapies

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Paul F Worth<sup>1,2</sup>

**To cite:** Worth PF. *Pract Neurol* 2013;**13**:140–152.

# What are the (motor) options?

- No change (“stick or twist”)
- Optimise mental/other health
- Therapists/day hospital
- PD specific
  - Tinker with the drugs
  - Complex therapies
    - Apomorphine
    - Intra-intestinal LD
    - Deep brain stimulation

# Drugs

- LD
  - CR, dispersible, standard
- Agonists
  - Standard, PR, patch
- COMTI
  - Entacapone
  - Opicapone
  - (tolcapone)
- MAO-BIs
  - Selegiline/rasagiline
  - Safinamide
- Amantadine

# Tinkering

- Wearing off
  - Fractionating
  - Adjunct
  - COMTI
- LIDs
  - Reduce DA drive?
  - Amantadine?
- Role of CR?

# How do you do it?

- No set formula
- Change one thing at a time
  - Low and slow
- Patients are brittle!
- Copy letters to patients
  - Be explicit
  - Contact for when things go pear shaped



# Complex therapies

- Age
- Carer?
- Burden of PD
  - Motor vs non-motor
  - Motor: LD responsive/induced?
  - Cognition and neuropsychiatric status
- Patient preference
- What is available

# The suitable CT candidate

- “Young”
- Willing/able carer
- Motor fluctuations are major problem
  - LD responsive (except tremor)
  - Exhausted tinkering
- No cognitive problems
- Patient, carer and you/team up for it

# Complex therapies: which one?

|                              | Apomorphine | Levodopa/carbidopa intestinal gel | Deep brain stimulation |
|------------------------------|-------------|-----------------------------------|------------------------|
| Age over 70 years            | +           | +                                 | -                      |
| Presence of comorbidities    | -           | +                                 | -                      |
| Severe speech disturbance    | +           | +                                 | -                      |
| Postural instability, falls  | 0           | 0                                 | -                      |
| Hallucinations/psychosis     | 0           | +                                 | +                      |
| Impulse control disorders    | 0           | +                                 | +                      |
| Excessive daytime sleepiness | -           | 0                                 | 0                      |
| Mild dementia                | 0           | 0                                 | -                      |
| Moderate-severe dementia     | -           | -                                 | -                      |
| Moderate-severe depression   | +           | +                                 | -                      |
| Previous suicide attempts    | 0           | 0                                 | -                      |
| Dysphagia                    | +           | +                                 | -                      |
| Weight gain                  | 0           | 0                                 | -                      |
| Restless legs                | +           | +                                 | 0                      |

# The future?

- Stem cells
  - Bona fide vs non-BF
  - Phase 1 study in Australia
  - Fetal cell trial (TRANSEURO)
- GDNF
- Viral vectors
- Other drugs (exenatide etc)

# Summary

- Complex PD
  - Motor fluctuations only part of it
  - .....yet that is what CT target
- Several factors determine suitability
  - Any complex therapy?
  - Which one?
- Sometimes, best option is conservative (palliative?)

# For patients/families

- Decide/agree upon your problems
  - .....*before* clinic.....
  - What troubles you the most?
  - The dreaded list
- Educate yourselves
  - ....don't be afraid to ask
  - We cannot read minds (yet)!