CHIEF SCIENTIST OFFICE

CODE: PCL/17/10

RESEARCH PROJECT BRIEFING

Improving predictions of prognosis in Parkinson's disease

AIMS

1. To develop a new database combining international cohorts of Parkinson's with low risk of bias.
2. To improve our understanding of how people with Parkinson's are affected over time.
3. To develop accurate individualised predictions of outcomes in Parkinson's.

KEY FINDINGS

- I have developed a pooled database of six European incidence cohorts including 1100 people with Parkinson's, with opportunities for many further high-quality research studies into the prognosis of Parkinson's
- I have identified important predictors of outcome in Parkinson's disease including a novel genetic predictor of death (apolipoprotein E epsilon 4 allele) and dependency (glucocerebrocidase gene polymorphisms).
- Work is ongoing to develop and validate robust prognostic models to predict risk of future outcomes for people at the time of their diagnosis of Parkinson's

WHAT DID THE STUDY INVOLVE?

I led a collaboration between investigators of six Parkinson's disease incidence cohorts to pool data from these studies and set up a database with highly detailed characterisation of 1100 participants. Data standardisation and checking and cleaning have ensured rigorous data quality. I then performed individual-patient-data meta-analysis to investigate prognosis in Parkinson's. I described key clinical outcomes in PD: development of balance impairment, dependency (the need for help with daily activities), dementia, and death). I then used survival analysis to identify key clinical and genetic predictors of these outcomes.

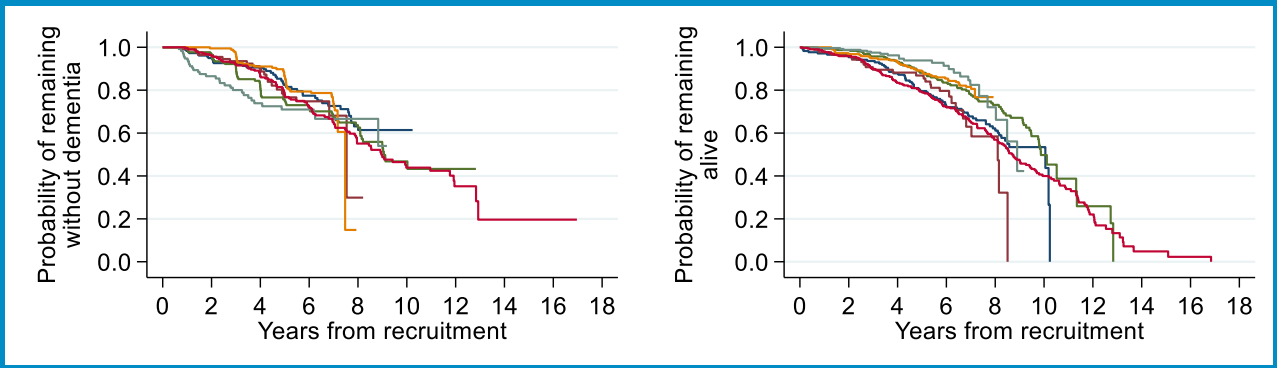
WHAT WERE THE RESULTS AND WHAT DO THEY MEAN?

Pooled outcome data were remarkably homogeneous between the included studies in the collaboration given previous heterogeneity in studies of these outcomes (see image). This demonstrates the value of incidence cohorts with low risk of bias.

The median time in years to balance impairment was 6.5 (95% confidence interval [CI] 5.6–6.8); to functional dependency was 6.0 (95% CI 5.5–6.5); to dementia was 10.0 (95% CI 9.0–12.0); and to death was 9.3 (8.6–9.8).

Key predictors of outcome included older age, male sex (for death), severity of parkinsonism and cognitive measures. Identification that apolipoprotein E epsilon 4 alleles have lower mortality and that glucocerebrocidase gene polymorphisms are associated with increased hazards of dependency were novel. Work is underway to combine these predictors to develop validated prognostic models to developed personalised predictions of these outcomes for individuals with Parkinson's.

Plots of the probabilities of remaining free from dementia and of remaining alive in the pooled PICC cohorts. Each line represents an individual study in PICC.



WHAT IMPACT COULD THE FINDINGS HAVE?

- More accurate information provision for people with Parkinson's and their relatives/carers
- Combining prognostic factors in validated prognostic models will enable:
  - Personalised medicine in Parkinson's disease – tailoring treatment to individuals
  - Improved efficiency of randomised clinical trials
  - Case-mix correction in comparisons of health outcomes e.g. between hospitals

HOW WILL THE OUTCOMES BE DISSEMINATED?

Results were presented at an International Congress of Parkinson's Disease and Movement Disorders in Hong Kong in 2018 and the World Parkinson's Congress in Kyoto in 2019.

Several research papers will ultimately be published from this fellowship. One paper has already been published in Parkinsonism and Related Disorders, another has been submitted, another drafted, and more are planned.

We will work with Parkinson's UK to update patient information sources in light of this work.

CONCLUSION

I have led an international collaboration to develop a large representative dataset with detailed characterisation of included participants. Identification of predictors of outcome and the development of robust validated prognostic models will hopefully lead to important benefits for patients with Parkinson's: reliable information about how they may be affected by it, treatment strategies tailored to individuals, and improved clinical trial design.

RESEARCH TEAM & CONTACT

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Additional Information

Completed August 2020. Funding received £76,000.