JNNP Online First, published on January 22, 2016 as 10.1136/jnnp-2015-312581

LETTER

Comparative epidemiology of incident Parkinson's disease in Cambridgeshire, UK

INTRODUCTION

Despite the increasing global importance of Parkinson's disease (PD), its exact incidence in the general population is not known. Comparing published studies, incidence rates from 1.5 to 19/100 000 person-years have been reported but such differences cannot simply be attributed to between-population differences in PD risk as no two studies have used the same case ascertainment strategy.[1] We have previously published the results of a community-based study of incident parkinsonism including PD in Cambridgeshire, UK: *CamPaIGN* (Cambridgeshire Incidence of PD from GP to Neurologist).[2] We now report the findings of a novel second incidence study in the same base population, using the same case ascertainment strategy: *PICNICS* (Parkinsonism: Incidence and Cognitive and Non-motor heterogeneity In CambridgeShire). This unique undertaking enables us to present a comparative analysis of these studies, representing the most complete set of PD incidence data yet reported in a defined population.

METHODS

The *PICNICS* study recruited newly diagnosed cases of PD and parkinsonism resident in Cambridgeshire between 1 April 2008 and 31 January 2010. Detailed methods including inclusion and exclusion criteria are available from the author. To summarise, case ascertainment was performed using a service-based screen of the normal routes of UK/National Health Service (NHS) healthcare referral. All general practitioners (GPs) and hospital specialists working with suspected/newly diagnosed PD operating in the county were regularly contacted by mail and electronically throughout the study period. They were instructed to refer all consenting cases of new/suspected PD or parkinsonism to the investigators.

Referrals were contacted and consenting participants were assessed in person by interview, examination and a battery of neuropsychological tests. Parkinsonism was defined by the presence of two of the four cardinal features of resting tremor, rigidity, bradykinaesia or postural instability and Idiopathic PD diagnosed by Queen Square Brain-Bank criteria. Cases of Incident PD were defined by the date of diagnosis. Published criteria were used to diagnose non-PD disorders wherever possible. 'Unspecified parkinsonism' labelled cases not fulfilling any such criteria. Participants entered longitudinal follow-up at 18-month intervals, allowing for diagnostic revision/refinement.

If patients declined participation, the source of referral, referral diagnosis, date of diagnosis by a specialist (if PD) and demographic details were recorded: no further contact was made.

Crude incidence rates were calculated as the number of cases per 100 000 person-years of screening, using demographic data for Cambridgeshire and applying direct age standardisation to the UK population structure (UK Office of National Statistics, 2008 estimates). Gender-adjusted incidence was calculated by standardising female incidence data to the male population structure. Statistical analysis was performed using SPSS V.14.0 and Open-Epi V.2

Local research ethics committee approval was obtained.

RESULTS

306 referrals were evaluated, of whom 24 did not meet inclusion criteria. Two hundred and eighty-two patients were contacted and 218 (77.3%) were assessed by the investigators. Two hundred and eleven cases of incident parkinsonism were identified, and 154 assessed in person. Of the 57 not assessed, 2 had been seen only in primary care. Therefore, 209/211 (99.0%) cases of incident parkinsonism were diagnosed by a specialist.

One hundred and seventy-two cases of idiopathic PD were identified at baseline, of which 127 were assessed. The remaining 45 had been diagnosed with PD by a specialist.

At 18 months, 115 cases of parkinsonism (109 PD) were available for follow-up evaluation leading to revision of diagnosis in 5 cases: 3 cases of 'atypical parkinsonism' were reclassified as PD and 2 cases of PD were reclassified. No further diagnostic revisions have occurred in ensuing follow-up. Diagnostic accuracy was thus 96.8%, an improvement on *CamPaIGN* (table 1).

Allowing for diagnostic revisions a final total of 211 cases of parkinsonism, and 173 cases of PD, were identified. These data are broken down by sex and age strata and compared with the equivalent data from *CamPaIGN* (table 1). The crude incidence for PD was 13.0 (10.9–15.1)/100 000 person-years and for parkinsonism 15.9 (13.8–18.2). Standardisation to the UK population gave figures of 15.8 (13.7–18.0, PD) and 18.8 (16.3–21.8, parkinsonism). Mean age at diagnosis was 68.6 (9.4) with an adjusted incidence ratio of M:F of 1.40, figures very close to those obtained in *CamPaIGN* (1.36).

DISCUSSION

We have shown that, using a prospective service-based method of case ascertainment, valid, accurate and reproducible estimates for PD incidence can be obtained. The data set from our consecutive studies (table 1) represents the most precise description of newly diagnosed PD in a defined population. Our updated incidence estimates figures are in agreement with two recent PD incidence studies, namely ICICLE-PD (15.9/100 000)[3] and the Norwegian ParkWest Study (12.6/100 000).[4]

UK data protection legislation precluded additional screening of healthcare records for further incident cases. However, we do not believe this had a significant impact on our results as current guidance to UK GPs stipulates that suspected PD should be assessed by a specialist within 6 weeks. The high percentage of referrals to *PICNICS* direct from primary care (34.9%) would indicate excellent adherence to this guidance, and the high percentage of primary care referrals also ensures that our cohort is representative. The existence of the 6-week target also means that the 12-week postcollection monitoring that we undertook after the end of the case collection period (31 January 2010) is likely to have been sufficient to capture any delayed referrals.

We were able to follow most cases longitudinally, and fewer than 4% of cases had their diagnosis revised at follow-up, although we allow that our follow-up rates for non-PD parkinsonism were less complete (6/27).

In *PICNICS*, PD incidence declined in the highest age strata, while in *CamPaIGN* a continued rise was observed. Notwithstanding that the identification of incident PD in the extreme elderly is complicated (difficulties with case ascertainment, diagnostic precision), understanding the relationship of PD incidence with age is important, both for healthcare economic modelling (should ageing populations plan for a rise in incident as well as prevalent PD?) and also as it may provide insights into the aetiology of the condition. The concept of Mild Parkinsonism in the Elderly has been proposed as a potential risk state for later PD, akin to MCI (Mild Cognitive Impairment) and Alzheimer's.[5] This is an area where epidemiological research will continue to

Table 1 Comparison of CamPaiGN and PICNICS' study results

	CamPaIGN	PICNICS
Recruitment period	2000–2002	2008–2010
Case collection duration (months)	25	21
N: PD (parkinsonism)	201 (309)	173 (211)
Response rate (%)	77.3%	76.0%
Diagnostic accuracy (%)*	86.4%	96.8%†
Follow-up duration	Up to 15 years	Up to 7 years
Primary care referrals (%)	23.3%	34.9%
Mean age at diagnosis PD (all/entering prospective FU)	72.0/67.8	68.6/68.3
Crude incidence parkinsonism (/100 000 person-years)	20.9 (18.7–23.3)†	15.9 (13.8–18.2)†
Crude incidence PD (/100 000 person-years)		
All	13.6 (11.8–15.6)†	13.0 (10.9–15.1)†
M	14.4	17.9
F	12.8	8.2
Unadjusted gender incidence ratio	1.13	2.16
Adjusted gender incidence ratio	1.36	1.40
PD incidence by age stratum (/100 000 person-years)		
30–39	0.9	0
40–49	2.0	2.0
50–59	9.6	14.9
60–69	41.2	43.2
70–79	75.5	79.7
80+	86.2	45.6
Delay diagnosis to assessment (months)	3.2 (4.8)	2.2 (2.7)
Symptom duration to assessment (months)	Not recorded	14.6 (2.8)
Medicated (Y:N)	68:74	68:60
Medication dose (if treated—LED mg)	374.8 (229.4)	315.5 (200.0)
Years of education	11.2 (3.1)	13.1 (2.8)
BDI	7.7 (5.7)	6.5 (4.1)
MMSE	28.0 (1.5)	28.4 (1.8)
ACE	NA	89.3 (8.1)
MDS-UPDRS (part 3)	26.4 (12.5)‡	31.5 (12.2)

*Calculated as sum of true positive and true negative as a percentage of the total number of cases assessed. Data below the serrated line refers to patients in each study who were recruited to long-term follow-up (n=142 (CamPaIGN), 128 (PICNICS).
†95% CI (Poisson distribution).
‡UPDRS (part 3) in CamPaIGN versus MDS-UPDRS, Unified Parkinson's Disease Rating Scale, MDS revision in PICNICS.
ACE, Addenbrookes Cognitive Examination; BDI, Beck Depression Inventory; CamPaIGN, Cambridgeshire PD Incidence from GP to Neurologist; FU, follow-up; LED, Levodopa Equivalent dose; MMSE, Mini-Mental State Examination; MDS-UPDRS, Unified Parkinson's disease Rating Scale, Movement-Disorders Society Revision; N, no; PD, Parkinson's disease; PICNICS, Parkinsonism: Incidence and Cognitive and Non-motor heterogeneity In CambridgeShire; Y, yes.

contribute to our understanding, complemented by insights from work on PD biomarkers and neuropathology.

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Contributors JRE wrote the manuscript which was reviewed and revised by the other authors. JRE, GCC and DPB performed data collection for the PICNICS study, and TF, CHW-G and SLM performed data collection for the CamPAiGN Study. Data analysis was performed by JRE (PICNICS) and TF and CHW-G (CamPaiGN).

Funding Cure Parkinson's Trust; Van Geest Foundation; Medical Research Council (RG38582); Parkinson's UK (RG39906); National Institute of Health Research Biomedical Research Centre Award to the University of Cambridge.

Competing interests None declared.

Ethics approval Essex 2 REC and Cambridgeshire 2 REC.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement The authors would be happy to consider collaboration and the sharing of longitudinal data with researchers working in the fields of PD natural history or biomarkers of progression in PD.

To cite Evans JR, Cummins G, Breen DP, *et al*. *J Neurol Neurosurg Psychiatry* Published Online First: [*please include* Day Month Year] doi:10.1136/jnnp-2015-312581

Received 27 October 2015
Revised 10 December 2015
Accepted 24 December 2015

J Neurol Neurosurg Psychiatry 2016;**0**:1–2. doi:10.1136/jnnp-2015-312581

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