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The Impact of Parkinsonian Syndromes on Carers over Time

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Abstract: The task of taking care of a parkinsonian's patient results in pressure on the carer themselves, which may have the adverse effect on their own health, social life and financial condition. The goal here is to compare the health of the carer at the point of diagnosis of the patient and to see how the health of the carer changes as the patients' disease progresses. The PINE study recruited patients who are newly diagnosed with parkinsonian syndromes and follow-up annually. Two patient diagnosis groups were created (Parkinson disease versus atypical parkinsonian syndromes) and comparisons of burden, mood and quality of life between the carers of these groups were undertaken. In this paper, we looked at the change in carer outcomes at various patient milestones: dementia, institutionalisation, motor fluctuation and dyskinesia. We also compared the health change of carer along with the follow up between two groups and find the factor which influences the carer' health change. The results shows that 194 carers were recruited (128 Parkinson's disease and 66 atypical parkinsonian syndromes) in the PINE study. Baseline carer characteristics were similar across the two groups. At baseline, the carer burden and depression level was higher in carers who had provided care longer and provided more care per day, carer' quality of life lowered and level of depression increased along with carer age, the level of quality of life has a negative relationship with the years known patients. The carer burden was higher for females compared to males and if the patient had an atypical parkinsonian syndrome rather than Parkinson disease. Carers who were employed had a higher quality of life and lower level of depression than those who had no job. The most important contributors to carer strain index (CSI) were upset that the person had changed (15.94 %), feeling overwhelmed (9.31 %) and confined (e.g. restricted free time) (9.49 %). During follow-up, the carer's CSI (P=0.002) and GDS-15 (P=0.004) was significantly worse after patients were diagnosed with dementia. The CSI and GDS-15 increased (higher burden and greater depression) and the EQ-5D decreased (lower quality of life) as follow-up increased. In conclusion, the carer' health status, quality of life and mood becomes worse as the patient parkinsonian syndromes progressed. The burden and depression level of the carer was significantly higher in the atypical parkinsonian syndromes group. These are important to provide guidance to the health management.

1. Background

Parkinsonian disorders are a group of neurodegenerative diseases characterised by tremor, stiffness and slowness, which increase with age. The commonest one, Parkinson's disease (PD), is the second most frequent neurodegenerative disease, affecting around 0.3% of the population worldwide [1]. Other atypical parkinsonian syndromes are rarer but more aggressive [2]. Over time, patients experience physical and cognitive decline and may need a carer to provide support in order to improve their quality of life [3]. Most carers are informal, such as a spouse, sibling or child. The informal carer can reduce the chance of early institutionalisation and the economic burden on the health system. According to statistics, the ageing population is increasing so the number of informal carers needed is likely to increase in order to meet needs [4]. The task of caregiving may result in greater pressure on the carer themselves which has an adverse effect on their own health, social life and financial condition [5]. Therefore, it is important to understand what factors impact on this carer pressure. This will help to provide a better support service or help with their own health needs in order to support them in their caregiving role [6].

Most previous research has focused on a single aspect such as the level of depression or the quality of life of the carer. However, the comprehensive analysis of the wellbeing of the carer can facilitate the most appropriate service to be complemented among them. The Parkinsonism Incidence in North-East Scotland (the PINE study) is a prospective follow-up study of newly diagnosed patients with parkinsonian syndromes and their carer from Aberdeen [7]. This study provides a unique opportunity to study the impact on the carer as the parkinsonian patient progresses in their disease.

Aims of this study:

1) To describe the baseline characteristics of carers at the point of diagnosis of patients;

2) Identify factors that influence the baseline health status of carers;

3) Assess whether carer outcomes are influenced by a patient milestone event (dementia, institutionalisation, dyskinesia and motor fluctuations), which often indicate a significant worsening of disease;

4) Describe how the carer outcomes change over time and see if it differs between those who care for people with Parkinson's disease and other parkinsonian syndromes.

2. Method

The PINE study is a prospective, life-long, observational study of an incident cohort of newly diagnosed parkinsonian syndromes (e.g. Parkinson's disease (PD) [8], Lewy body dementia (DLB) [9], progressive supranuclear palsy (PSP) [10], multisystem atrophy (MSA) [11], corticobasal degeneration (CBD) [12] and vascular parkinsonism [13]) from 315,000 residents registered in 37 primary care practices in Aberdeen, Scotland over a 4.5 year period. Detailed recruitment methods are described elsewhere [7]. All consenting eligible participants were offered the option of asking a carer to take part in the study and both patient and carer were followed-up annually at clinic or at home until the death of the patient.

At each annual review, the precise parkinsonian syndrome was classified by a single consultant neurologist with movement disorders expertise using all available clinical information and applying the appropriate research criteria available at the time for PD, DLB, MSA, PSP, CBD and vascular parkinsonism. Some of those who died the final diagnosis was confirmed with the post-mortem.

2.1 Assessments/outcome measures

At baseline, demographic data collected on patients included: age at diagnosis, gender, ethnic group, marital status, whether they live alone. For the carers: gender, relation to patient, how long they have been caring for the patient, how many hours per day they required care, years known the patient.

Patients and carers were followed up yearly at a clinic appointment. Various patient outcomes were collected but we are interested in the milestone events: date of dementia, date of institutionalisation (e.g. nursing home as no longer able to be cared for at home), date of development of motor fluctuations (i.e. a switch between mobility and immobility) and date of dyskinesia (i.e. impairment of voluntary movement).

At each annual visit, the carers were asked to complete the following questionnaires:

1) The EQ-5D-5L including the EQ-5D visual analogue score (VAS) representing the patient's self-rated health out of 100 and the EQ-5D utility score which scores five domains to give a societal-based health status [14]

2) The 15-item Geriatric Depression Scale (GDS-15) which is a measure of depression/mood among the elderly [15]

3) The Care Strain Index (CSI) including the score from 13 aspects of carer burden (inconvenience, sleep disturbance, physical strain, confining lifestyle, family adjustments, change to personal plans, demands on time, emotional adjustments, upsetting behaviour, upset due to changes from patient's former self, work adjustments, financial strain and feeling overwhelmed) individually and a combined total [16]

2.2 Statistical Analysis

Data were extracted from PINE study database on 4 April 2018. Some initial data cleaning occurred and corrections made after discussion with the data custodian. We chose the eligible patients from the database and divided them into those with idiopathic Parkinson disease (PD) and those with atypical parkinsonian syndromes (APS) (patients with DLB, PSP, CBD, vascular parkinsonism, unspecified parkinsonism and other parkinsonism). As we interested in the comparison of carer outcomes over time, it was not relevant to include data for a second or thirds carer after a change (e.g. original carer died). Therefore, carer outcomes were censored after a change in carer, and only information for the first carer used.

Firstly, the carers were divided into two groups based on the patient diagnosis (PD versus APS) and the baseline characteristics were summarised. The continuous variables were described by the mean (standard deviation) or the median (interquartile range (IQR)) if skewed. The categorical variables were presented by the frequency and percentage.

For each of the carer outcomes at baseline (CSI, GDS-15 and EQ-5D), we presented median (IQR) by a number of demographic characteristics: for the patient: their diagnosis, education level, gender and marital state; for the carer: age, gender, relation to patient, employment status, years they had known the patient, how long they had needed to give care, and how many hours per day. These summary statistics were compared across the levels of the characteristics using an appropriate statistical test. If the data were normally distributed, the independent sample t-test or one-way ANOVA was applied, otherwise, the Mann-Whitney test or Kruskal Wallis test was used. We utilised a significance level of $p<0.05$ throughout the analysis. After that, we choose the variables which are significant ($p<0.05$) to undertake a linear regression analysis for the four scales independently and checked assumptions of them. Additionally, the percentage of 13 items within the CSI instrument is represented by the pie chart.

To compare the carer outcome of four scales before and after each patient milestone event, we choose data from the year prior to an event and the year following an event for every patient who had an event. The paired t-test was used when the data of difference is normally distributed, if not, the Wilcoxon matched paired test will be used. Moreover, we use the median (IQR) to compare the value of four scales between the before and after patient milestone event.

To assess carer outcomes over time, we displayed the carer outcome at each time point in a line graph (baseline to 8 years). To assess if outcomes changed over time, or differed between diagnosis groups we used a mixed model which allowed for the repeated observations for each carer.

The PINE study was approved by the NHS Grampian Research Ethics Committee and the Multicentre Research Ethics Committee A for Scotland, also agreed to include patients with dementia who lacked the capacity to consent with a guardian's assent. This analysis required no additional ethics review.

3. Results

3.1 Baseline characteristics

Of 346 patients who meet the eligibility requirement for the PINE study, 194 patients had a carer who gave consent for follow-up. Those carers were divided into two group according to the diagnosis of patients: PD (n=128) and APS (n=66) (Figure 1). Most of the carers in the two groups are female and elderly with similar age, the main relationship between patient and carer was the spouse (99 (77.3%) in the PD group and 43 (65.2%) in the APS group). More people in the APS group needed care at baseline and for more hours per day than the PD group (Table 1).

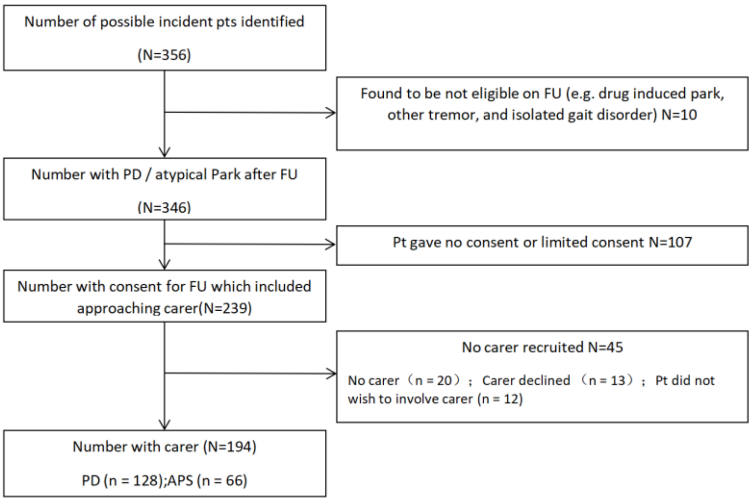

Figure 1: Flow diagram for included carers of PINE study

Table 1: Baseline characteristic of carers split by patient diagnosis group.

		Parkinson's disease(PD) (n=128)	**atypical parkinsonian syndromes (APS) (n=66)**
Age (IQR)[a]		70 (56, 75)	67.5 (53.75, 77.00)
Female		94 (73.4%)	53 (80.3%)
Relation to patient	**Partner**	99 (77.3%)	43 (65.2%)
	Child	21 (16.4%)	22 (33.3%)
	Other	8 (6.4%)	1 (1.5%)
Years known the patient (IQR) [b]	**Partner**	52.00 (43.00, 59.00)	51.50 (45.00, 60.00)
	Child	50.00 (46.00, 52.00)	48.50 (45.00, 55.00)
	Other	42.50 (23.50, 61.50)	45.00 (45.00, 45.00)
Hours per day caring (IQR) [c]		0.50 (0, 1.50)	1.0 (0.20, 2.00)
How long they have been caring for the patient [d]	**=< 12 month**	47 (37.3%)	31 (47%)
	>12 months	29 (23%)	23 (34.8%)
	Help not required	50 (39.7%)	12 (18.2%)
Patient not Live alone [e]		94 (80.3%)	39 (73.6%)
a Missing n=2 PD b Missing n=1APS c Missing n=4 PD, n=3APS d Missing n= 2 PD e Missing n=11 PD, n= 13APS			

3.2 Comparison of baseline carer outcomes for patient and carer characteristics

Table 2 describes the comparison of baseline characteristics and their relationship to baseline carer quality of life (EQ-5D utility score and EQ-5D VAS). There were no differences in these quality of life scores for the patient characteristics. Older carers had lower EQ-5D scores (p<0.001), with those in employment showing a higher quality of life (p<0.001). Retired carers and those unemployed had similar EQ-5D profiles. Carers who were the patient's partner showed the lowest QoL for the utility score, but there was no difference for the VAS score.

Table 2 also describes associations for GDS-15 and baseline characteristics. The score showed no difference across different patient characteristics, but it increased with the carers' age (P=0.023), the time of caring every day (P=0.003), the number of years they had required care (P=0.024), and for unemployed carers (P<0.001).

Table 2: Patient and carer characteristics: description of QoL (EQ-5D) 、carer mood (GDS-15) and carer burden (CSI) at baseline

					EQ-5D utility score		EQ-5D VAS		GDS-15		CSI	
		group	**N available**	**N total**	**IQR**	**Sig (p-value)**	**IQR**	**Sig (p-value)**	**IQR**	**Sig (p-value)**	**IQR**	**Sig (p-value)**
patients	**Last diagnosis [a]**	**PD**	121	128	0.85(0.73, 1.00)	0.649	80.00(70.00, 90.00)	0.798	2.00 (0.00, 4.00)	0.246	3.00 (1.00, 7.00)	< 0.001
		APS	63	66	0.85 (0.69, 1.00)		80.00 (70.00, 90.00)		2.00 (1.00, 5.00)		8.00 (3.00, 11.00)	
	Education [a]	**Primary, secondary**	134	143	0.85 (0.73, 1.00)	0.215	80.00 (70.00, 90.00)	0.171	2.00 (1.00, 4.00)	0.063	5.00 (1.00, 9.00)	0.385
		tertiary	49	50	1.00 (0.71, 1.00)		85.00(76.00, 94.50)		1.00 (0.00, 3.00)		4.00(1.00, 9.00)	
	Gender [a]	**Female**	64	65	5.00 (1.00, 8.00)	0.301	80.00 (77.25, 90.00)	0.566	1.00 (0.00, 4.00)	0.203	0.85 (0.74, 1.00)	0.454
		Male	120	129	5.00 (1.25, 9.00)		80.00 (70.00, 90.00)		2.00 (1.00, 4.00)		0.85 (0.73, 1.00)	
	Marital State [b]	**Married**	128	135	0.80 (0.73, 1.00)	0.464	80.00 (70.00, 90.00)	0.556	2.00 (0.00, 4.00)	0.833	4.00 (1.00, 8.00)	0.082
		Divorced	2	3	0.90 (0.80, ..)		83.50 (77.00, …)				8.50 (5.00, …)	
		Single	5	5	0.80 (0.74, 0.92)		83.00 (77.50, 92.50)		1.00 (0.50, 5.00)		1.00 (0.00, 12.00)	
		Widowed	46	48	0.85 (0.80, 1.00)		80.00 (79.75, 90.00)		1.00 (0.00, 4.25)		6.00 (2.00, 10.00)	
		Cohabiting	1	1								
		Separated	2	2	0.84 (0.69, ..)		70.00 (50.00, ..)		4.00 (2.00, ..)		7.00 (2.00,…)	
carer	**Age [b]**	**<49**	27	29	1.00 (0.85, 1.00)	<0.001	90.00 (80.88, 98.00)	0.001	1.00 (0.00, 4.00)	0.023	5.00 (2.00, 10.00)	0.125
		50-59	32	32	1.00 (0.85, 1.00)		88.00 (80.00, 95.00)		1.00 (0.00, 2.75)		5.00 (2.00, 12.00)	
		60-69	34	36	0.85 (0.69, 1.00)		90.00 (70.00, 95.00)		2.00 (0.00, 4.00)		7.00 (2.75, 10.00)	
		70-79	69	72	0.80 (0.69, 1.00)		80.00 (70.00, 90.00)		2.00 (1.00, 4.00)		2.00 (1.00, 7.00)	
		>=80	22	23	0.76 (0.69, 1.00)		80.00 (68.75, 82.50)		3.00 (1.00, 4.00)		5.50 (1.75, 9.25)	
	Gender [a]	**Female**	139	147	0.85 (0.73, 1.00)	0.615	80.00 (70.00, 90.00)	0.720	2.00 (1.00, 4.00)	0.507	5.00 (2.00, 10.00)	0.006
		Male	45	47	0.80 (0.73, 1.00)		80.00 (75.00, 90.00)		1.00 (0.00, 4.00)		3.00 (1.00, 6.00)	
	Relation to patient [b]	**Partner**	135	142	0.80 (0.73, 1.00)	0.039	80.00 (70.00, 90.00)	0.130	2.00 (1.00, 4.00)	0.348	5.00 (1.00, 9.00)	0.137
		Child	40	43	0.92 (0.80, 1.00)		85.50 (80.00, 92.50)		1.00 (0.00, 3.00)		5.50 (2.00, 10.00)	
		Other	9	9	1.00 (0.80, 1.00)		83.00 (80.00, 92.50)		1.00 (0.00, 3.50)		5.00 (0.50, 9.50)	
	Employment [b]	**No**	12	12	0.78 (0.66, 0.96)	<0.001	81.50 (76.00, 90.00)	0.001	3.00 (1.00, 5.00)	<0.001	7.50 (2.50, 9.75)	0.199
		Yes	56	58	1.00 (0.85, 1.00)		90.00 (80.00, 97.00)		1.00 (0.00, 2.00)		5.00 (2.00, 9.75)	
		Retired	115	121	0.80 (0.69, 1.00)		80.00 (70.00, 90.00)		2.00(1.00, 4.00)		5.00 (1.00, 9.00)	
	Years known the patient [b]	**<=30**	17	17	1.00 (0.76, 1.00)	0.002	90.00 (75.00, 98.00)	0.023	1.00 (0.00, 4.00)	0.371	5.00 (1.00, 11.00)	0.155
		31-40	24	24	1.00 (0.80, 1.00)		85.00 (77.25, 95.00)		2.00 (0.00, 4.00)		3.50 (0.25, 7.00)	
		41-50	44	48	1.00 (0.80, 1.00)		90.00 (75.25, 97.00)		1.00 (0.00, 3.00)		5.00 (2.00, 10.00)	
		51-60	75	79	0.80 (0.73, 1.00)		80.00 (70.00, 90.00)		2.00 (1.00, 4.00)		5.00 (2.00, 8.00)	
		>=60	4	5	0.86 (0.65, 1.00)		67.50 (61.25, 77.50)		3.00 (1.25, 4.00)		1.00 (0.25, 2.50)	
	How long they have been caring for the patient [b]	**Help not required**	60	62	1.00 (0.73, 1.00)	0.211	87.50 (75.00, 96.75)	0.024	1.00 (0.00, 3.00)	0.024	2.00 (1.00, 3.75)	<0.001
		<=12 months	75	78	0.85 (0.73, 1.00)		80.00 (75.00, 90.00)		2.00 (1.00, 4.00)		6.00 (2.00, 9.00)	
		>12 months	49	52	0.80 (0.69, 1.00)		80.00 (70.00, 90.00)		3.00 (1.00, 4.00)		8.00 (5.00, 13.00)	
	Hours per day helping [b]	**0**	60	60	1.00 (0.73, 1.00)	0.078	82.50 (71.25, 95.75)	0.403	1.00 (0.00, 4.00)	0.003	2.00 (1.00, 5.00)	<0.001
		<=1	71	74	0.85 (0.73, 1.00)		80.00 (75.00, 90.00)		1.00 (0.00, 4.00)		5.00 (1.00, 8.00)	
		1.001-2	28	30	0.80 (0.69, 0.96)		80.00 (70.00, 90.00)		3.00 (2.00, 5.00)		9.00 (6.25, 12.75)	
		2.001-3	4	4	1.00 (0.85, 1.00)		83.00 (68.75, 96.50)		0.50 (0.00, 1.00)		3.50 (1.25, 11.75)	
		>=3.001	18	19	0.80 (0.69, 0.89)		80.00 (68.75, 90.00)		3.00 (1.00, 4.25)		9.00 (5.00, 13.00)	

a: Mann-Whitney test b: Kruskal Wallis test

The relationship between carer burden (CSI) and baseline factors can be seen in the Table 2. Those caring for people with APS had a higher burden than for PD (P<0.001) and the female carer showed higher burden than male (P=0.006). The burden was increased as the hours per day helping (P<0.001) or the year of caring (P<0.001) increased. In the 13 contributors of CSI instrument, the fact that the patient had changed from their former self accounted for 15.94% which ranked first among all problem, the next was that caring was confining (e.g. free time was restricted) (9.49%), then a feeling of being overwhelmed (9.31%). Financial strain (2.76%)

and work adjustments (3.13%) contributed least to CSI (Figure 2).

Table 3: Linear regression model results for CSI, EQ-5D and GDS-15 at baseline

	Estimate	**95% CI**	**p-value**
CSI (R^2 = 0.30)			<0.001
Constant	2.65	0.77, 4.52	0.006
Hours per day caring	0.25	0.06, 0.43	0.010
Diagnosis (PD)	-1.81	-3.12, -0.49	0.008
How long they have been caring for the patient : < 12 months	4.37	2.62, 6.12	<0.001
How long they have been caring for the patient : > 12 months	2.85	1.38, 4.32	<0.001
Gender = female	1.91	0.50, 3.33	0.008
EQ-5D utility score (R^2=0.13)			<0.001
Constant	1.05	0.79, 1.32	<0.001
Age of carer	-0.004	-0.01, 0.00	0.068
Relation to the patient: partner	-0.001	-0.13, 0.13	0.992
Relation to the patient: child	-0.08	-0.22, 0.06	0.274
Employment: no	-0.05	-0.17, 0.07	0.423
Employment: yes	0.10	0.01, 0.19	0.032
Years known the patient	0.001	-0.002, 0.004	0.538
EQ-5D VAS (R^2=0.10)			0.004
Constant	98.66	79.79, 117.54	<0.001
Age of carer	-0.23	-0.51, 0.05	0.107
Employment: no	0.37	-9.48, 10.22	0.942
Employment: yes	2.86	-4.46, 10.18	0.441
Years known the patient	-0.04	-0.24, 0.16	0.690
How long they have been caring for the patient : < 12 months	-2.72	-7.88, 2.43	0.299
How long they have been caring for the patient : > 12 months	-4.99	-10.78, 0.81	0.091
GDS-15 (R^2=0.12)			<0.001
Constant	2.40	-0.88, 5.67	0.150
Age of carer	0.00	-0.04, 0.04	0.987
Employment: no	0.67	-0.96, 2.30	0.420
Employment: yes	-1.35	-2.60, -0.09	0.036
Hours per day caring	0.10	-0.01, 0.22	0.073
How long they have been caring for the patient : < 12 months	0.67	-0.19, 1.53	0.128
How long they have been caring for the patient : > 12 months	0.17	-0.86, 1.19	0.753

Table 3 shows the linear regression for four carer outcomes as dependent variables. Carers showed higher burden (CSI) at baseline if they cared for longer per day, were caring for APS patients, were female and already caring for the patient for long time. In the model for the EQ5D utility score, significant independent predictors were: age, relation to the patient, employment status and years known patient, but explained only 13% of variability. The carers who had known the patient for a long time, were unemployed, older, or patient' spouse showed worse health condition in this model. In terms of EQ-5D VAS, the independent predictor variables were age of carer, how many years they had known the patient, employment and how long they had required care, but this just accounted for 10% of the variability. In this model, the carer who did not need to help the patient had about a 5 point higher score than those who had needed to give help for more than 12 months, whilst carer who was retired had about a 3 point lower score than an employed carer when other independent variables remained unchanged. Additionally, the score of EQ-5D VAS decreased with carer 'age and the years known the patient. 12% of the variability in carer depression scores (GDS-15) were explained by age, employment and hours per day caring. The carer who was working had lower level of depression (2.02 points) than one with no job, moreover, the depression increased along with the age of carer and the time caring every day.

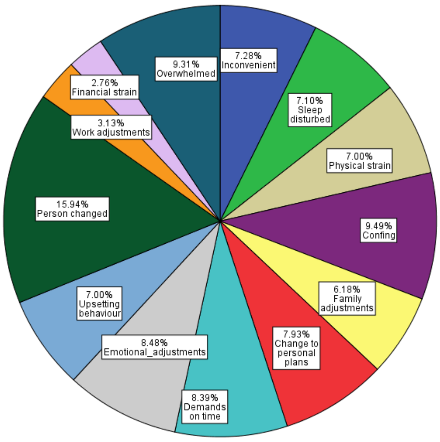

Figure 2: percentage contribution of each of the 13 carer burden items to the total score

3.3 Compare carer outcome before and after one of the patient milestone events

Table 4: Comparison of carer outcome before and after a patient milestone event

		Group	Median (IQR)	Median (IQR) of difference	Sig ^{a} (p-value)
Institutionalization	**CSI**	**after**	8.00 (5.00, 14.00)	-1.00 (-4.50, 1.00)	0.173
		before	10.00 (8.00, 14.00)		
	EQ-5D utility score	**after**	0.85 (0.80,1.00)	0.00 (0.00, 0.03)	0.180
		before	0.80 (0.73, 0.85)		
	EQ-5D VAS	**after**	88.00 (80.00, 90.00)	4.50 (-0.25, 9.25)	0.080
		before	70.00 (60.00, 85.00)		
	GDS-15	**after**	2.00 (0.00, 4.00)	-1.00 (-1.75, 1.75)	0.831
		before	3.00 (2.00, 4.00)		
Dementia	**CSI**	**after**	10.00 (5.00 ,13.00)	2.00 (-1.00, 6.00)	0.002
		before	7.00 (4.00, 10.00)		
	EQ-5D utility score	**after**	0.80 (0.69, 1.00)	0.00 (-0.07, 0.00)	0.331
		before	0.80 (0.69, 1.00)		
	EQ-5D VAS	**after**	80.00 (64.00, 90.00)	-4.00 (-13.75, 4.25)	0.065
		before	80.00 (70.00, 90.00)		
	GDS-15	**after**	2.00 (1.00, 5.00)	1.00 (-5.00, 3.00)	0.004
		before	2.00 (1.00, 3.00)		
Motor fluctuation	**CSI**	**after**	6.50 (4.00, 12.00)	0.55 (-1.75, 3.50)	0.193
		before	6.00 (4.00, 11.50)		
	EQ-5D utility score	**after**	0.73 (0.69, 1.00)	0.00 (-0.10, 0.00)	0.575
		before	0.80 (0.71, 0.92)		
	EQ-5D VAS	**after**	85.00 (70.00, 90.00)	2.50 (-5.50, 7.50)	0.753
		before	79.50 (71.00, 90.00)		
	GDS-15	**after**	2.00 (1.00, 3.00)	0.00 (-1.00, 0.00)	0.719
		before	2.00 (0.50, 4.00)		
Dyskinesia	**CSI**	**after**	5.00 (2.00, 8.00)	0.50 (-1.00, 2.00)	0.261
		before	4.00 (1.00, 7.00)		
	EQ-5D utility score	**after**	0.80 (0.69, 1.00)	0.00 (-0.20, 0.00)	0.058
		before	1.00 (0.80, 1.00)		
	EQ-5D VAS	**after**	86.50 (69.00, 90.00)	-3.00 (-10.00, 0.00)	0.063
		before	80.00 (70.00, 93.00)		
	GDS-15	**after**	2.00 (1.00, 3.00)	0.00 (-1.00, 0.00)	0.639
		before	2.00 (0.00, 4.00)		

a: Wilcoxon matched pairs test

From the Table 4, there is no significant difference in the carer outcome between before and after patients' institutionalisation or development of motor fluctuation or dyskinesia, but the carer had significantly worse CSI (2.00 (-1.00, 6.00)) or GDS-15 (1.00 (-5.00, 3.00)) after their patient was diagnosed with dementia than before. The carer had slightly lower (worse) grades of EQ-5D VAS (-3.00 (-10.00, 0.00)) after their patient developed dyskinesia.

3.4 Comparison of carer outcomes over time

Table 5 and Table 6 shows that the number of carers included at each follow-up declines with time, especially in the APS group. This is due to the fact that when a patient dies, the carer is no longer followed-up.

Figure 3 shows a slight declining trend in carer quality of life (EQ-5D utility and VAS) over the follow-up period, however this was not a significant decline over time (p=0.901 utility, p = 0.800 VAS). For the VAS score there was no difference between diagnostics groups, and no interaction between group and time (Table 7). However, for the utility score, and overall difference in the groups can be found (p=0.02). We need to be wary of this interpretation because the number of observations beyond four years is quite small (n< 10) for the APS group (Table 5).

Table 5: Number of carers with outcome at each assessment.

		EQ-5D utility score	EQ-5D VAS	GDS-15	CSI
baseline	**PD**	124	123	123	123
	APS	66	66	65	64
1st visit	**PD**	112	112	111	113
	APS	51	51	51	47
2nd visit	**PD**	109	109	109	109
	APS	38	38	38	36
3nd visit	**PD**	95	95	95	95
	APS	26	26	26	26
4nd visit	**PD**	86	86	85	86
	APS	16	16	16	16
5nd visit	**PD**	77	76	77	77
	APS	10	10	10	10
6nd visit	**PD**	70	70	66	68
	APS	8	8	7	7
7nd visit	**PD**	59	59	40	57
	APS	7	7	3	7
8nd visit	**PD**	50	50	21	48
	APS	1	1	0	1

Carer depression scores differed between the two groups, but did not differ significantly over time (p=0.515) and there was no interaction effect (Table 6).

Table 6: Number of carers with each CSI item at each assessment

		Inconvenient	Sleep disturbed	Physical strain	Confining	Family adjustments	Change to personal plans	Demands on time	Emotional adjustments	Upsetting behaviour	Person changed	Work adjustments	Financial strain	Overwhelmed
baseline	**PD**	125	125	125	125	125	125	124	125	124	125	125	124	125
	APS	65	65	65	65	65	65	66	66	66	66	65	66	66
1st visit	**PD**	114	114	114	114	114	114	114	114	114	114	114	113	114
	APS	51	51	51	51	51	49	50	51	50	51	50	51	51
2nd visit	**PD**	109	109	109	109	109	109	109	109	109	109	109	109	109
	APS	37	37	37	37	37	37	37	37	37	36	37	37	37
3nd visit	**PD**	96	96	96	96	96	96	96	96	95	96	96	96	96
	APS	26	26	26	26	26	26	26	26	26	26	26	26	26
4nd visit	**PD**	86	86	86	86	86	86	86	86	86	86	86	86	86
	APS	16	16	16	16	16	16	16	16	16	16	16	16	16
5nd visit	**PD**	77	77	77	77	77	77	77	77	77	77	77	77	77
	APS	10	10	10	10	10	10	10	10	10	10	10	10	10
6nd visit	**PD**	70	70	70	69	70	70	70	70	69	70	70	70	70
	APS	7	7	7	7	7	7	7	7	7	7	7	7	7
7nd visit	**PD**	59	58	59	59	59	59	59	59	59	59	58	59	59
	APS	7	7	7	7	7	7	7	7	7	7	7	7	7
8nd visit	**PD**	52	52	52	52	52	52	52	51	51	52	51	51	52
	APS	1	1	1	1	1	1	1	1	1	1	1	1	1

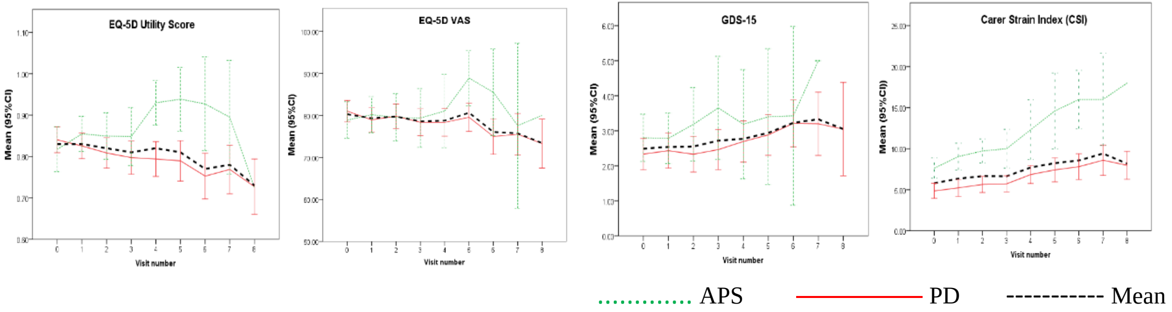

Figure 3: Outcome of carers at each time point by diagnosis group

Figure 3 shows that the CSI increases with time, i.e. burden is increasing and this is a significant increase (p<0.001). There was a difference between groups overall, but the change over time did not differ between the groups (p=0.214) (Table 7).

Table 7: Results of mixed model: comparison over carer outcomes over timea

	Time (p-value)	**Diagnosis group (p-value)**	**Interaction of time and diagnosis group (p-value)**
EQ-5D utility score	0.901	0.020	0.081
EQ-5D VAS	0.800	0.208	0.504
GDS-15	0.515	0.020	0.951
CSI	<0.001	< 0.001	0.214
a: Mixed Model Analysis (Type III Tests of Fixed Effects)			

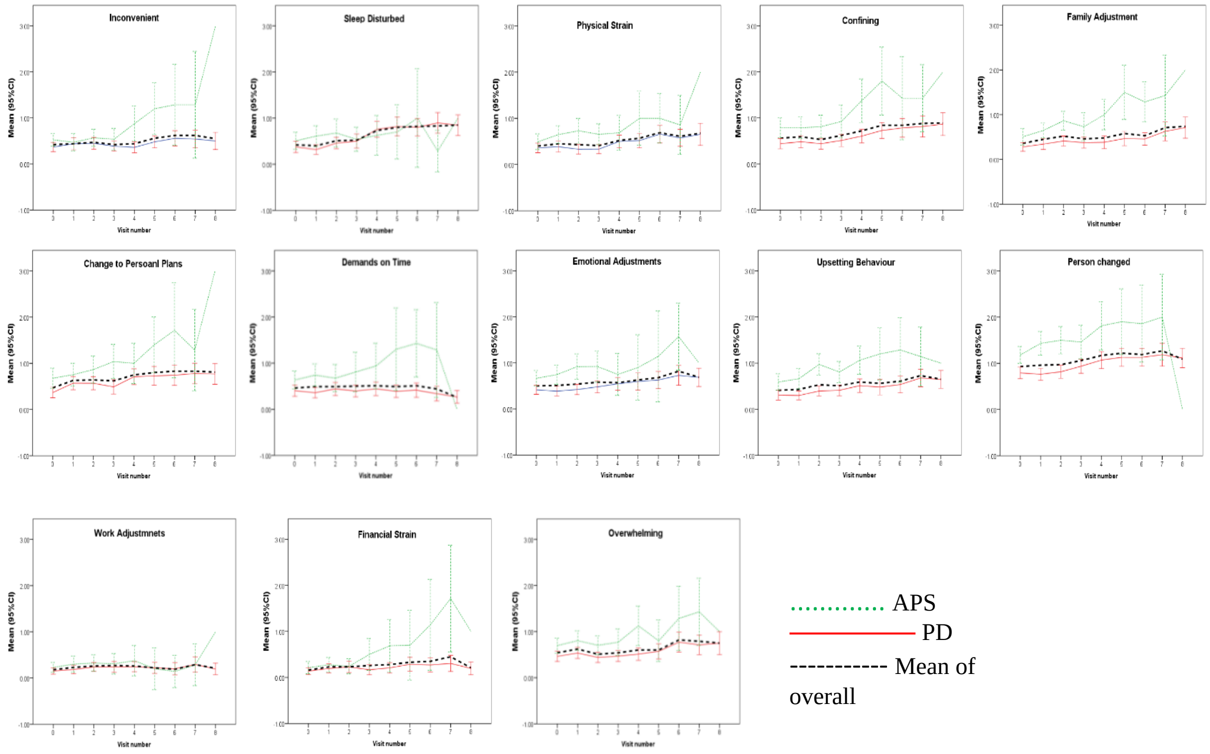

Figure 4: Mean (95% CI) score for each CSI element by time (CSI) at each time point by group

Table 8: Results of mixed model: comparison over carer burden items over time [a]

	Time (p-value)	**Diagnosis group (p-value)**	**Interaction of time and diagnosis group (p-value)**
Inconvenient	<0.001	<0.001	<0.001
Sleep disturbed	0.066	0.868	0.263
Physical strain	0.026	<0.001	0.639
Confining	<0.001	<0.001	0.162
Family adjustments	<0.001	<0.001	0.023
Change to personal plans	<0.001	<0.001	0.142
Demands on time	0.012	<0.001	0.013
Emotional adjustments	0.014	<0.001	0.640
Upsetting behavior	<0.001	<0.001	0.501
Person changed	<0.001	<0.001	0.250
Work adjustments	0.473	0.060	0.882
Financial strain	<0.001	<0.001	<0.001
Overwhelmed	0.018	0.002	0.668
a: Mixed Model Analysis (Type III Tests of Fixed Effects)			

In terms of the 13 elements of CSI, all of them increased along with the visit time and the score was significantly higher in the APS group than PD group except sleep disturbed and work adjustments. Only four elements had significant interaction effect of time and diagnosis group. Inconvenience (p<0.001) and financial strain (p<0.001) worsened more quickly for the APS group in particular after 3 years (Figure 4). A greater amount of family adjustment as needed for the APS group more quickly than the PD group (p = 0.023). Linked to all of those demands on time also showed a significant interaction of time and diagnosis group, with the APS group showing a quicker increase in demands on time (p = 0.013) (Table 8).

4. Discussion

In terms of parkinsonian syndromes, the percentage of female carers is significantly higher than men due to 1) the prevalence of parkinsonian is higher in men than women [17] and most carers were spouses; 2) the percentage of men serve as the primary carer to their unhealthy partner is higher than vice versa according to statistics [18]. Women have been reported to have more carer burden than men, such as secondary stressors (relational and financial problems, problems combining different tasks and heavier workload) [19].

The symptoms of parkinsonian syndromes, such as motor problem, mood disturbance and communication problem, always worsen with increasing age among the patients [20]. This trend will bring the challenge to carers' tasks and disrupt their normal life and results in increasing carer' burden and depression and worsen health. APS tends to progress more rapidly than PD in terms of motor and cognitive features like early falling, hallucination or dementia. These are associated with more difficulty in caring, so carer in the APS group had a higher level of burden and depression than in the PD group as shown by our data [2]. Unexpectedly, the carer of the patient with APS increased the quality of life over time in this studybut this is probably a spurious finding due to the small number of carer/patients pairs surviving more than 3 years.

Carers did not have better reported burden, mood or quality of life after patient institutionalisation, which is different from previous research [21]. This may be because carers in this study were older people with additional co-morbidity [22]. This phenomenon was supported by the fact that young carers who were employed also had better health status and mood than retired old people in this study. Unexpectedly, there was no significant difference in carer burden between different ages, which is different with other literature [23], but it is consistent with there being no difference between the employed young people and retired old people.

In terms of the burden of caregiving in patients diagnosed with PD or APS, the biggest problem was upset to the carer because the person cared for had changed from their former self, for example, the patients will slowly show disruptive behavior (disinhibition, aggression and agitation), delusions and mood disturbance. These symptoms will influence mood of patients and increases the difficulty in caring, especially after diagnosed with dementia [24]. Moreover, the task of taking care of patients will restrict carer' free time, which can influence their normal social activities and personal plans, such as quitting a job and giving up travel on holiday. Although carers with no job may have financial stress and mental pressure which can influence their health condition and mood [25], there was a low percentage of carer complaints in this study about work adjustments, such as taking time off to care for the patients with some financial strain. This was because most of our carers were already retired and seemed to have adequate financial support.

4.1 Limitation

The PINE is a long-term observational study of the prognosis of an incident cohort of newly diagnosed with parkinsonian patients in which carers were also recruited and followed up. This kind of design is the best way of studying prognosis [7], but this study was restricted to Aberdeen and not all patients had carers for various reasons (usually lack of consent), which may result in selection bias and reduce the generalizability to other places, especially the countries with different formal care systems. Due to the nature of disease, the numbers available at each follow-up declined and this can impact on the representativeness of the data, particularly in the APS group who tend to die earlier. Moreover, some analysis can’t rule out the confounder of age. The APS is difficult to distinguish from Parkinson’s i.e. diagnostic uncertainty [2], but this cannot be avoided in clinical studies of parkinsonism and we applied strict diagnostic criteria. Further study is needed to make generalizations to other geographic locations and consider additional confounding variables (e.g. care comorbidity, disease severity in patients, formal care support etc.). How health systems can support informal caregivers in this setting and other health conditions is important and should be considered in future studies.

5. Conclusion

We assessed the impact of parkinsonian syndromes on the carer from diagnosis over a period of 8 years. Carers had a higher burden if caring for patients in the APS group or after the patient developed dementia. Development of dementia in the patient was also shown to impact on carer depression, showing an increase after the diagnosis. Overall, the patient’ burden, mood and QoL become worse over time, especially the CSI. The main burden comes from upset over how the patient changes, feeling confined and overwhelmed. Few carers complained about having to make work adjustment or financial strain. Carers who were employed also had better health status and mood than retired people. This research suggests that healthcare systems needs to assess ways to provide carers with psychological counseling and training about special caring to see if this improves carer outcomes and reduces burden over time. The impact of increased formal care also need to be assessed.

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