Drugs - Real World Outcomes (2024) 11:1–11
https://doi.org/10.1007/s40801-023-00410-1

ORIGINAL RESEARCH ARTICLE

Economic Burden of Parkinson's Disease: A Multinational, Real-World, Cost-of-Illness Study

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Accepted: 26 November 2023 / Published online: 9 January 2024

Abstract

Background Parkinson's disease is now one of the fastest-growing neurodegenerative disorders in the developed world, with an increasing prevalence and associated socioeconomic costs. Progression of the disease leads to a gradual deterioration in patients' quality of life, despite optimal treatment, and both medical and societal needs increase, often with the assistance of paid and/or unpaid caregivers.

Objective We aimed to quantify the incremental economic burden of Parkinson's disease by disease severity in a real-world setting across differing geographic regions.

Methods Demographics, clinical characteristics, health status, patient quality of life, caregiver burden, and healthcare resource utilization data were drawn from the Adelphi Parkinson's Disease Specific Program™, conducted in the USA, five European countries, and Japan.

Results A total of 563 neurologists provided data for 5299 individuals with Parkinson's disease; 61% were male, with a mean age of 64 years. Approximately 15% of individuals were deemed to have advanced disease, with significantly more comorbidities, and a poorer quality of life, than those with non-advanced disease. Overall, the mean annual healthcare resource utilization increased significantly with advancing disease, and resulted in a three-fold difference in the USA and Europe. The main drivers behind the high economic burden included hospitalizations, prescription medications, and indirect costs.

Conclusions People with Parkinson's disease, and their caregivers, incur a higher economic burden as their disease progresses. Future interventions that can control symptoms or slow disease progression could reduce the burden on people with Parkinson's disease and their caregivers, whilst also substantially impacting societal costs.

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Key Points for Decision Makers

Analysis confirmed that individuals with Parkinson's disease, and their caregivers, experienced a substantial and incrementally higher economic burden as their disease progressed.

Recognition of the economic burden of advanced Parkinson's disease may help to drive earlier optimization of treatments, thereby timely preventing financial burdens and improving health outcomes.

1 Introduction

Parkinson's disease (PD) is among the world's fastest-growing neurodegenerative disorders [1–3]. From 1990 to 2016, the number of people with PD doubled to more than 6 million, with

over 200,000 PD-related deaths globally [4]. Over this period, there was an increase of 22% in the age-standardized prevalence globally, and estimates for the number of Parkinson's cases in 2040 range from 12 to 17 million [5]. The increase in prevalence has been attributed partly to the aging of the population, to a longer disease duration, possible changes in environmental or social risk factors, and to increased recognition and diagnosis in routine medical care [2].

Beyond the motor manifestations, PD is associated with a range of other symptoms. These may affect the gastrointestinal system, autonomic nervous system, sleeping patterns, and mood or cognition, and contribute to a reduced quality of life and significant disability [6, 7].

As the disease progresses, some individuals with PD become increasingly dependent on care, frequently provided by non-professional persons. The burden experienced by caregivers correlates with various disease aspects, including the duration of disease and caregiving, and non-motor symptoms such as sleep problems, anxiety, or depression [8, 9]. In addition to substantial occupational restrictions [10], caregiver burden can result in reduced time spent with family or in leisure and social activities, sleep impairment, and anxiety or depression [11].

In a study using a human capital approach to estimate the future burden of PD on the US economy, the largest indirect costs were found to be the future loss of income due to PD-related premature morbidity and secondary mortality, loss of income from reduced employment, absenteeism, and early retirement [10]. A study in people with PD receiving Medicare showed those with advanced disease had a higher economic burden when compared with those with mild or moderate disease [12]. These studies have identified the need for further understanding of the incremental economic burden in higher disease severity in differing healthcare systems [4, 10]. However, other than lost productivity, the economic burden associated with PD remains poorly defined and, in particular, how it changes with disease progression.

1.1 Objectives

The objective of this study was to quantify the incremental economic burden of PD by disease severity using data from a large cohort of people with PD managed in a real-world setting in differing international geographic regions.

2 Materials and Methods

2.1 Study Design

Data were derived from the Adelphi Real World Parkinson's Disease Specific Programme (DSP™). The DSP was a cross-sectional survey with elements of a retrospective analysis of people with PD and their treating physicians and caregivers, conducted in France, Germany, Italy, Spain, the UK, and the USA between 2017 and 2022. The DSP methodology and its general applicability have been previously described [13, 14].

A geographically representative sample of physicians were recruited to participate in the DSP by local fieldwork agents, following completion of a short screening questionnaire. In order to be eligible to participate in the DSP survey, physicians were required to have been in clinical practice between 5 and 35 years and to be personally responsible for treatment decisions of at least three patients with PD per week. Patients were required to be over the age of 18 years and have a physician-confirmed diagnosis of PD.

Physicians completed an online patient record form for their 12 next consecutively consulting patients who visited them for routine care, to mitigate against selection bias and to provide a sample reflective of individuals presenting in a real-world clinical setting. Completion of the patient record forms was undertaken through consultation of existing patient clinical records, as well as the judgment and diagnostic skills of the respondent physician, consistent with decisions made in routine clinical practice. All survey materials were translated from English into the local language by local fieldwork agents, according to a defined protocol. Each patient record form took approximately 25 min to complete.

These record forms collected data relating to patient demographics, clinical characteristics, and disease history, as well as comorbidities as indexed by the Charlson Comorbidity Index [15]. Patients' disease severity was also rated by physicians though two clinical rating scales; the Unified Parkinson's Disease Rating Scale (UPDRS) as well as the Movement Disorder Society additions (MDS-UPDRS) [16, 17]. Cognitive impairment was assessed through the Mini-Mental State Examination [18]. Patients were grouped into early, intermediate, or advanced disease according to their physician's clinical judgment. As participating physicians were required to see a minimum of three patients with PD per week, all were considered highly experienced and could reasonably be expected to accurately distinguish the degree of PD severity.

The patient record form also contained questions used to estimate healthcare utilizations, covering the number of annual hospitalizations, emergency room visits, consultations, scans, professional and respite care, prescription medications, and indirect costs. Each patient for whom the physician completed a record form was then invited to voluntarily complete a pen-and-paper patient-reported questionnaire, and upon agreement provide their informed consent to participate. Patients were asked to assess their quality of life using the Parkinson's Disease Questionnaire-39 item (PDQ-39) [19–21]. For individuals who had

a caregiver (formal or informal), the caregivers were also invited to voluntarily complete a questionnaire to assess the burden of providing care as measured by the Zarit Burden Interview [22]. Patient and caregiver questionnaires took approximately 20 min to complete. Patient-reported questionnaires were completed by the patient independently from their physician and were returned in a sealed envelope, ensuring the patient's responses were kept confidential from their physician.

2.2 Ethical Considerations

Using a checkbox, patients provided informed consent to take part in the survey. Data were collected in such a way that patients and physicians could not be identified directly, and no personally identifiable data were collected. Physician and patient data were pseudo-anonymized. A code was assigned when data were collected. Upon receipt by the study team, data were pseudo-anonymized again to mitigate against tracing them back to the individual. Data were aggregated before being shared with the researchers and/or publication. The DSP follows all relevant market research guidelines and complies with the Health Insurance Portability and Accountability Act and equivalent European Union European Pharmaceutical Marketing Research Association guidelines [23, 24], and because of the nature of the data, the collection and aggregation did not require ethics committee approval. The DSP and all questionnaires therein were granted an exemption following a review by the Western Institutional Review Board (Puyallup, WA, USA) on 3 July, 2019 (AG8689).

2.3 Data Analysis

Categorical variables are reported as number and percentages. Continuous variables are reported as means and standard deviations or medians and interquartile range. Odds ratios (ORs) modeling whether costs were zero or not were estimated through logistic regression. Mean disease costs were estimated using two-part regression analyses (Logit and Inverse Gaussian/Log), accounting for zero observations and adjusted for country, age, sex, and the Charlson Comorbidity Index. All analyses were conducted in Stata version 17.0 (StataCorp LLC, College Station, TX, USA).

Patients were eligible for inclusion in this analysis if they were taking oral therapy for PD, and naive to treatment with device-aided therapy (DAT). The economic burden was based on annual healthcare resource utilization related to PD, with local costs applied to the individual resource use together with indirect costs. Indirect costs were measured as the impact on the employment status of patients' non-professional caregivers (whether they had stopped working or reduced their hours) and were calculated using the mean hourly wage and mean weekly hours worked in each region. Annual costs in Europe were based on UK National Health Service reference costs and were converted to Euros using 2020 currency rates. Costs in the USA were based on 2020 Medicare reference data and reported in US Dollars. Costs in Japan were based on a review of the literature conducted during 2021, and reported in Japanese Yen.

3 Results

3.1 Patient Demographics

A total of 563 neurologists provided data for 5299 individuals with PD (USA 28%, France 11%, Germany 13%, Italy 12%, Spain 13%, UK 13%, and Japan 12%; Table 1, Fig. 1). Of these, 2104 individuals completed the voluntary self-reported questionnaire (USA 38%, Europe 46%, Japan 16%). Data were also collected from a total of 875 caregivers (USA 23%, Europe 63%, and Japan 14%). The population with PD was predominantly male (61%) overall, with most individuals aged 65 years or more (71%) with a similar mean age (64–67 years) at diagnosis in the early/intermediate and advanced PD groups (Table 1).

One third (33%) of individuals in the early/intermediate disease group had a clinical diagnosis of 2 years or less (mean 3.6 ± 3.8 years), while over half (54%) of those with advanced disease had been diagnosed for 6 years or more (mean 9.3 ± 5.3 years; Table 1). The proportions of individuals determined by physicians to have early/intermediate or advanced disease were similar across all countries (early/intermediate 85% and advanced 15% overall; Table 1). Three quarters of individuals determined to have early/intermediate PD (75%) were at Hoehn and Yahr stage I/II, while over 90% of those determined to have advanced PD were at Hoehn and Yahr stage III–V [25]. Individuals at an advanced stage also had significantly more comorbidities than those at an early/intermediate stage (mean 2.8 ± 2.3 and 1.7 ± 1.6, respectively), of which approximately 10% were considered to be moderate to severe compared with 2% in the early/intermediate group (Table 1).

3.2 Disease Status and Caregiver Burden

Overall disease control, as measured by the total UPDRS and MDS-UPDRS scores, and cognitive impairment using the Mini-Mental State Examination, were significantly worse in the advanced PD group compared with the early/intermediate group (UPDRS 53.1 vs 29.0, MDS-UPDRS 48.4 vs 31.1, and Mini-Mental State Examination 21.3 vs 25.3, respectively; all $p < 0.001$; Table 2). Individuals with advanced disease also rated their quality of life as to be poorer than in

those with early/intermediate disease (PDQ-39 40.9 vs 25.3, respectively), indicating reduced functioning and well-being [26] (Table 2). The humanistic burden in caregivers of individuals with advanced PD, as measured by the Zarit Burden Interview, was significantly greater than for individuals at an early/intermediate stage, with approximately 40% reporting a moderate-to-severe burden compared with 23% with the early/intermediate group (Table 2).

3.3 Healthcare Resource Utilization

People with advanced disease were considerably more likely to incur direct costs than those with early disease, even when adjusted for confounders, with greater resource utilization in terms of hospitalization rate (OR: USA 10.4; Europe 8.6, Japan 1.2; Table 3) and professional care, such as district nurse, nursing home staff, home help, psychiatric nurse, physiotherapist, speech therapist, or social worker (OR: USA 20.7; Europe 25.6; Japan 1.3; Table 3). The increase in total indirect costs in people with advanced disease, including non-professional care, with a reduction in weekly working hours because of caregiving incurred by a spouse, son/daughter, other relative, or friend, was greater in Europe than in the USA or Japan (OR: 14.7, 10.0, and 1.0, respectively; Table 3). In addition, emergency room visits and respite care were more frequent among individuals with advanced disease than with early disease in all regions (Table 3).

3.4 Healthcare Resource Utilization Costs

Overall, mean annual PD-related healthcare resource utilization costs estimated from the two-part regression model (Logit and Inverse Gaussian/Log) increased significantly with progressing disease (Table 4). Mean annual costs rose approximately two-fold to three-fold in individuals with advanced disease in the USA and Europe compared with those with intermediate disease ($35,287 vs $14,988 and €15,628 vs €5864, respectively), with a smaller increase in Japan (JPY 1,695,963 vs 1,219,426, respectively; Table 4). The cost of resource use in individuals with advanced disease was consistently high across all the countries (Table S1 of the Electronic Supplementary Material).

The distribution of annual costs per patient showed similar patterns in the USA and Europe and patterns within each region. The main drivers behind the high annual costs among individuals with advanced PD in each region included hospitalizations and prescription medications, whilst people at all stages of disease in the USA incurred higher emergency room costs than in Europe and Japan (Fig. 2). People in Japan with early PD had a higher proportion of hospitalizations and indirect costs than either the USA or Europe, while the cost of respite care was higher in Europe (Fig. 2). People with advanced disease in each region had fewer consultations than those with earlier disease, whilst scans were also used less frequently in the advanced disease stage in each geographic region.

4 Discussion

Our real-world study was an evaluation and comparison of the economic burden of individuals with PD receiving care in the USA, Europe, and Japan. The analysis confirmed that individuals with PD and their caregivers experience a substantial and incrementally higher economic burden as their disease progresses, with a greater use of professional and respite care in the USA and Europe than in Japan. This finding is consistent with previous studies and emphasizes the increasing economic burden associated with disease progression.

Our findings appear to be reflected across other countries not included as part of this study. Research from Australia found that the overall costs associated with more severe disease were almost four times those for mild disease, largely driven by hospitalizations and professional care [27]. Results from Sweden align with our findings in Europe, with similar studies finding that professional care was a leading driver of costs at later stages of disease [28, 29], as well as observing an overall increase in costs with worsening disease severity [30]. A study from Brazil also found that overall costs increased with worsening disease severity [31].

The global prevalence of PD has more than doubled between 1990 and 2016 [2], although some differences in prevalence by sex and geographic location have been reported [32]. This increase has been attributed to the aging of the population and increasing life expectancy, increased urbanization, exposure to environmental toxins through occupation and increasing industrialization and reductions in the number of smokers [1, 5]. Many people diagnosed with PD in both Europe and the USA do not see a neurologist or specialist geriatrician [33, 34] and better engagement with specialist healthcare providers, including regular reviews of medication use, may reduce the current healthcare burden of PD [33].

Indeed, a model of the course of PD showed that reducing progression rates could produce a significant economic benefit through a decrease in direct medical costs, an increase in quality adjusted life-years, and a decrease in lost income [35]. This finding was consistent with a similar study of Medicare beneficiaries in the USA, which found disease-related costs for those with advanced disease were over twice as high as for those with mild or moderate PD across all categories of medical expenses, and patients with severe disease were also more likely to incur primary disease-related medical costs [12]. A further study of individuals

Table 1 Demographic details of individuals with Parkinson's disease, by disease severity

	Overall	Early/Int	Advanced	*p*-Value
Country, *n* (%)	5299 (100.0)	4494 (84.8)	805 (15.3)	< 0.001
USA	1478 (27.9)	1243 (27.7)	235 (29.2)	
France	560 (10.6)	466 (10.4)	94 (11.7)	
Germany	712 (13.4)	602 (13.4)	110 (13.7)	
Italy	620 (11.7)	560 (12.5)	60 (7.5)	
Spain	623 (11.8)	551 (12.3)	72 (8.9)	
UK	680 (12.8)	562 (12.5)	118 (14.7)	
Japan	626 (11.8)	510 (11.3)	116 (14.4)	
Patient sex, *n* (%)	5299	4494	805	
Male	3215 (60.7)	2728 (60.7)	487 (60.5)	0.938
Female	2084 (39.3)	1766 (39.3)	318 (39.5)	
Patient age (years), *n* (%)	5299	4494	805	
≥ 65	3748 (70.7)	3018 (67.2)	730 (90.7)	< 0.001
Age at diagnosis	4199	3639	560	
Mean (SD)	64.4 (10.4)	64.1 (10.4)	66.6 (9.9)	< 0.001
Time since diagnosis (years)	4199	3639	560	
Mean (SD)	4.4 (4.5)	3.6 (3.8)	9.3 (5.3)	< 0.001
0–2	1473 (28.5)	1440 (33.1)	33 (4.1)	
3–5	1212 (23.5)	1124 (25.8)	88 (11.0)	
6–10	907 (17.6)	700 (16.1)	207 (25.8)	
> 10	468 (9.1)	238 (5.5)	230 (28.6)	
Missing	1100 (21.3)	855 (19.6)	245 (30.5)	
Current Hoehn and Yahr, *n* (%)	5299	4494	805	< 0.001
1	1741 (32.9)	1727 (38.4)	14 (1.7)	
2	1715 (32.4)	1655 (36.8)	60 (7.5)	
3	1094 (20.6)	910 (20.2)	184 (22.9)	
4	541 (10.2)	185 (4.1)	356 (44.2)	
5	208 (3.9)	17 (0.4)	191 (23.7)	
Number of comorbidities	5299	4494	805	
Mean (SD)	1.8 (1.8)	1.7 (1.6)	2.8 (2.3)	< 0.001
0	1321 (24.9)	1214 (27.0)	107 (13.3)	
1	1385 (26.1)	1234 (27.5)	151 (18.8)	
2–3	1799 (33.9)	1496 (33.3)	303 (37.6)	
4 +	794 (15.0)	550 (12.2)	244 (30.3)	
Charlson Comorbidity Index	5299	4494	805	
Mean (SD)	0.4 (1.0)	0.3 (0.8)	1 (1.5)	< 0.001
None (score 0)	4205 (79.4)	3772 (83.9)	433 (53.8)	
Mild (score 1–2)	900 (17.0)	613 (13.6)	287 (35.7)	
Moderate (score 3–4)	146 (2.8)	85 (1.9)	61 (7.6)	
Severe (score 5 +)	48 (0.9)	24 (0.5)	24 (3.0)	

Int intermediate, *SD* standard deviation

with PD in the UK that examined the incremental costs of advanced disease compared with mild-to-moderate disease in the UK National Health Service from 1993 to 2013 found that costs in patients with advanced disease were higher by an average of £1069 ($1608) per patient than those without advanced PD [36].

The significant economic cost, as well as patient and caregiver burdens highlighted in this study emphasize the need for early and comprehensive disease control. Although attempts have been made to define advanced PD [37], the adoption of appropriate therapies among these patients may be hindered by a lack of consensus.

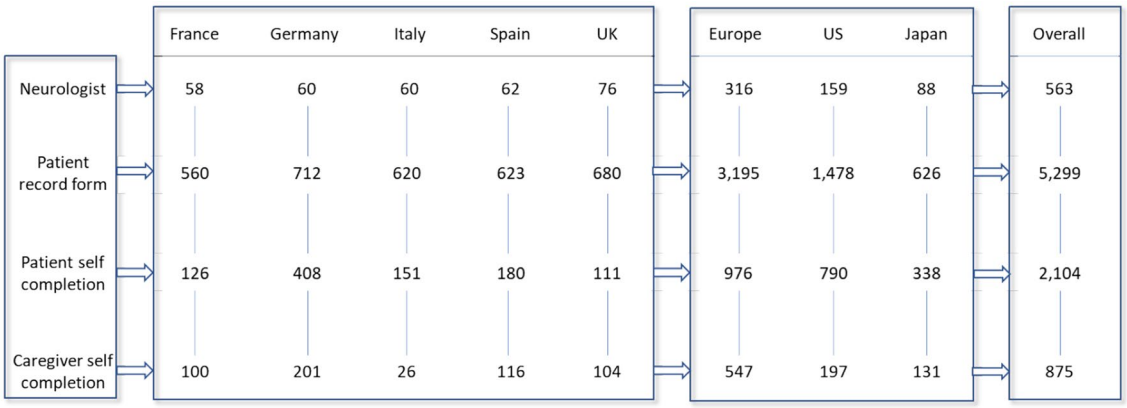

Fig. 1 Total number of respondents by country, by region (Europe, USA [US], and Japan) and overall

Table 2 Health status of individuals with Parkinson's disease, and caregiver burden, by disease severity

	Overall	Early/Int	Advanced	*p*-value
Physician rating				
Most recent UPDRS score	1064	936	128	
Mean (SD)	31.9 (27.2)	29.0 (24.3)	53.1 (36.2)	< 0.001
Most recent MDS-UPDRS score	338	294	44	
Mean (SD)	33.3 (26.7)	31.1 (25.3)	48.4 (31.0)	< 0.001
Most recent MMSE score	1231	968	263	
Mean (SD)	24.4 (4.8)	25.3 (4.3)	21.3 (5.3)	< 0.001
Patient rating				
PDQ-39	1869	1618	251	
Mean (SD)	27.4 (18.3)	25.3 (17.3)	40.9 (18.5)	< 0.001
Caregiver rating				
Zarit Burden Interview	853	669	184	
Mean (SD)	28.6 (17.7)	27.2 (17.1)	33.5 (19.2)	< 0.001
No burden (0–20)	317 (37.2)	262 (39.2)	55 (29.9)	
Mild to moderate (21–40)	305 (35.8)	250 (37.4)	55 (29.9)	
Moderate to severe (41–60)	192 (22.5)	132 (19.7)	60 (32.6)	
Severe (61 +)	39 (4.6)	25 (3.7)	14 (7.6)	

Int Intermediate, *MDS* Movement Disorder Society, *MMS* Mini Mental State Examination, *PDQ-39* Parkinson's Disease Questionnaire (39 items), *SD* standard deviation, *UPDRS* Unified Parkinson's Disease Rating Scale

Treatments for advanced PD rely largely on levodopa, but clinical guidelines also recommend other non-levodopa pharmaceuticals impacting on the dopamine system, such as monoamine oxidase B or catechol-O-methyltransferase inhibitors [38]. However, data suggest patients with advanced disease may not be adequately controlled on oral therapy alone [39, 40], highlighting the need for DAT. Device-aided therapy options that have shown clinical efficacy include levodopa-carbidopa gel [39], deep brain stimulation [41], or various formulations of apomorphine [42]. Our data highlight the societal burden of advanced PD. Better recognition of the economic burden of advanced disease may promote novel interventions and improved optimization of treatment in the future, improving health outcomes and reducing the healthcare burden on people with PD, their caregivers, and society.

Table 3 Annual healthcare resource utilization costs in individuals with intermediate and advanced compared with early Parkinson's disease as base (odds ratio and 95% CIs) by geographic region

	USA					Europe					Japan				
	n	Inter	95% CI	Adv	95% CI	*n*	Inter	95% CI	Adv	95% CI	*n*	Inter	95% CI	Adv	95% CI
Hospitalization	1340	2.43	1.03–5.73	10.36	4.32–24.85	2883	3.75	2.68–5.27	8.62	5.81–12.78	521	0.68	0.37–1.24	1.21	0.60–2.42
ER visits	1478	3.16	1.66–6.02	8.84	4.45–17.54	3195	2.78	1.97–3.92	4.82	3.24–7.16	626	0.63	0.25–1.59	1.65	0.60–4.59
Consultations	1478	1.29	0.77–2.16	0.81	0.40–1.61	3195	1.44	1.08–1.92	0.87	0.58–1.29	626	1.52	0.90–2.58	2.23	0.97–5.12
Scans	1478	0.50	0.40–0.64	0.44	0.31–0.64	3195	0.60	0.51–0.71	0.46	0.35–0.59	626	1.07	0.73–1.55	1.07	0.65–1.76
Professional care	1393	6.21	2.43–15.87	20.65	7.91–53.94	3078	7.26	4.11–12.82	25.62	14.31–45.87	597	1.02	0.61–1.70	1.34	0.73–2.48
Respite care	1424	4.88	0.60–39.63	28.22	3.56–223.75	2980	4.73	2.95–7.59	12.46	7.44–20.87	556	0.92	0.49–1.73	0.90	0.39–2.08
Prescriptions	1478	1.00	1.00–1.00	1.70	0.21–13.38	3195	2.68	1.38–5.22	1.93	0.91–4.13	626	7.29	0.90–59.00	1.94	0.23–16.62
Total indirect costs[a]	1442	2.66	0.95–7.47	10.03	3.35–30.07	3062	5.22	2.79–9.78	14.65	7.34–29.24	596	0.73	0.33–1.62	0.98	0.36–2.67
Total costs	1478	1.00	1.00–1.00	1.00	1.00–1.00	3195	1.00	1.00–1.00	1	1.00–1.00	626	1.00	1.00–1.00	1.00	1.00–1.00

Adv, dvanced, *CI* confidence interval, *ER* emergency room, *Inter* intermediate

[a]Indirect costs included non-professional care measured by the impact on a caregiver's employment status

4.1 Limitations

We recognize some limitations of this research in that this was a non-interventional study, with physicians completing forms on consecutive individuals with PD. Selection bias was possible owing to the fact that the neurologists surveyed represent a pragmatic sample based on those willing to participate in the DSP and may not be representative of the overall population of physicians treating people with PD. Additionally, the voluntary nature of the patient and caregiver-reported questionnaires meant that smaller samples were inevitably collected for these outcomes, potentially reducing the comparability of certain results. Use of physician-reported data to estimate indirect costs negated these sample issues when modeling costs. However, the information they provided may have been less accurate than that from the patients/caregivers themselves, and some degree of under-estimation or over-estimation of these costs is likely. Total costs of direct and indirect resource use were evaluated without taking into account differences in insurance coverage between countries, and related differences in out-of-pocket costs, as this information was not available.

Identification of the target patient group was also based on the judgment of the respondent physician and not a formalized diagnostic checklist, but was considered representative of the physician's real-world classification of the patient. However, the individuals with PD who participated in the survey may not reflect the general PD population, as those who were more severely affected may not have been able to participate. Nevertheless, as our study involved a relatively large number of neurologists from different geographical regions in the USA, Europe, and Japan, it is likely that the findings are representative of the real-world management of people with PD in those countries.

5 Conclusions

This study demonstrated that, in the USA, Europe and Japan, people with PD experience a substantial and incrementally higher economic burden as their disease progresses. Future interventions that alleviate the burden of PD-associated symptoms and delay progression could reduce the economic burden. Moreover, the recognition of the increased symptom burden of people with advanced PD may allow more timely optimization of disease management.

Table 4 Estimated mean annual aggregated per patient costs by severity of Parkinson's disease (adjusted for country, age, sex, and Charlson Comorbidity Index) in differing geographic regions

	USA (USD)				Europe (Euros)				Japan (JPY)			
	n	Early	Inter	Adv	*n*	Early	Inter	Adv	*n*	Early	Inter	Adv
Hospitalization												
Mean	1340	87	360	1750	2883	106	544	1514	521	225,929	169,975	250,025
95% CI		18–156	189–532	918–2581		65–146	421–667	1044–1983		114,631–337,227	73,374–266,576	88,347–411,702
ER visits												
Mean	1478	1205	3069	8131	3195	8	26	52	626	1157	616	2382
95% CI		371–2039	2042–4097	5057–11,205		5–11	21–32	38–66		263–2051	79–1154	134–4630
Consultations												
Mean	1478	427	570	624	3195	228	287	341	626	48,880	56,894	80,779
95% CI		397–456	533–608	544–704		212–244	266–307	294–388		39,843–57,918	47,000–66,789	53,871–107,686
Scans												
Mean	1478	387	303	245	3195	217	134	99	626	37,784	31,057	34,131
95% CI		317–456	242–364	150–340		195–239	119–149	78–121		31,26–44,300	26,466–35,649	25,715–42,548
Professional care												
Mean	1393	148	1053	4145	3078	251	2125	7980	597	113,724	228,941	61,817
95% CI		− 15 to 310	648–1457	2174–6117		71–431	1454–2796	5405–10,555		− 21,611 to 249,059	− 54,130 to 512,013	7135–116,500
Respite care												
Mean	1424	63	433	1535	2980	203	1022	2199	556	6633	7628	5876
95% CI		− 81 to 206	34–831	236–2834		82–324	718–1326	1490–2908		3225–10,040	3642–11,614	1375–10,377
Total indirect costs[a]												
Mean	1478	164	536	1942	3195	151	722	2031	626	151,701	145,633	200,953
95% CI		12–317	251–821	887–2998		59–242	499–944	1313–2750		67,905–235,496	55,786–235,480	35,202–366,704
Prescriptions												
Mean	1442	5198	8664	16,915	3062	548	1005	1466	596	159,409	578,682	1,060,000
95% CI		4534–5861	7467–9861	11,092–22,738		507–589	904–1105	1180–1753		132,441–186,377	406,84–750,522	463,635–1,660,000
Total costs												
Mean	1478	7679	14,988	35,287	3195	1712	5865	15,682	626	745,217	1,219,426	1,695,963
95% CI		7326–9751	13,040–17,721	20,015–52,362		2110–2709	6993–10,800	8700–43,404		563,932–819,277	841,569–1,370,000	893,879–2,050,000

Adv advanced, *CI* confidence interval, *ER* emergency room, *Inter* intermediate

[a]Indirect costs included non-professional care measured by the impact on a caregiver's employment status

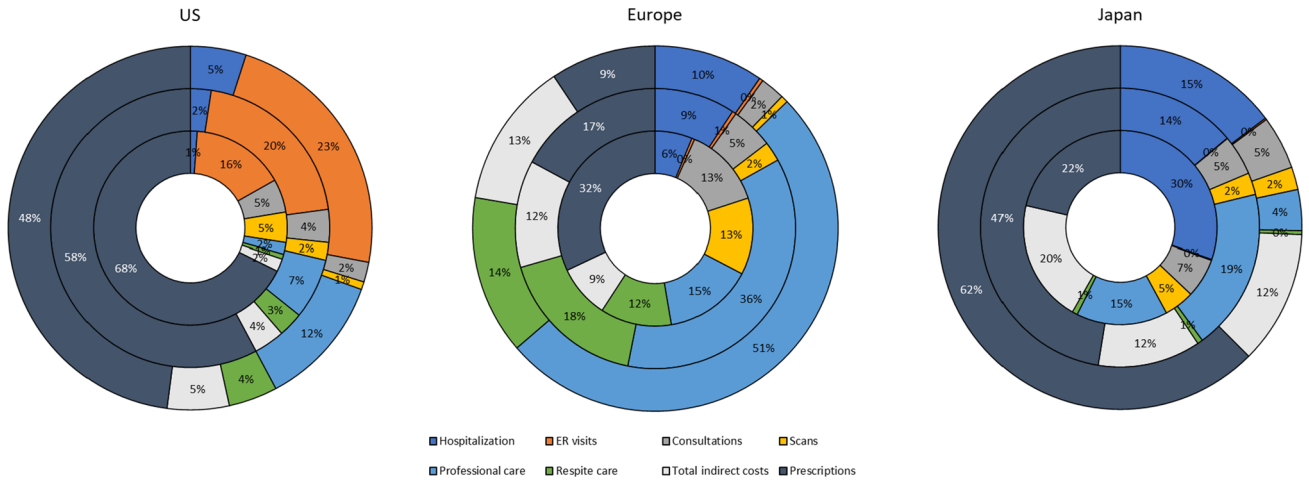

Fig. 2 Distribution of healthcare resource utilization costs per patient with Parkinson's disease, by severity (inner ring, early; middle ring, intermediate; and outer ring, advanced disease) and geographic region. *ER* emergency room, *US* USA

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40801-023-00410-1.

Acknowledgements The authors acknowledge Yash J. Jalundhwala, an employee of AbbVie, for his input into the study design and interpretation of the results. The authors acknowledge Weiwei Xu, an employee of IQVIA, and Matthew Madin-Warburton and Seyavash Najlerahim, former employees of IQVIA for their contribution to the study design, which was funded by AbbVie. The authors acknowledge James Pike, an employee of Adelphi Real World, for his support conducting the data analysis. The authors also acknowledge Connie H. Yan and Zachary Baldwin for their assistance in the preparation of this manuscript. Medical writing assistance was provided by K. Ian Johnson, BSc MBPS SRPharmS, Harrogate House, Macclesfield, UK. This assistance was funded by AbbVie. All the individuals mentioned gave their permission to be named in the Acknowledgments section.

Author Contributions Study conception and design: AA, PLK, VSC, JCP, TY, JO. Data collection and analysis: JW. Interpretation of results: KRC, J-PA, PO, SL, JD, AA, PLK, VSC, JCP, TY, JO, JW, PM-M. Review of all drafts of the manuscript: KRC, J-PA, PO, SL, JD, AA, PLK, VSC, JCP, TY, JO, JW, PM-M. Approval of the final draft for publication: KRC, J-PA, PO, SL, JD, AA, PLK, VSC, JCP, TY, JO, JW, PM-M. All named authors take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Funding Data collection was undertaken by Adelphi Real World as part of an independent survey, entitled the Adelphi Real World Parkinson's Disease Specific Programme (DSP). The analysis described here used data from the Adelphi Real World Parkinson's DSP, which is a wholly owned Adelphi Real World product. AbbVie was one of multiple subscribers to the DSP. AbbVie did not influence the original survey through either contribution to the design of questionnaires or data collection. AbbVie participated in the interpretation of the data, review, and approval of the manuscript. All authors contributed to the development of the manuscript and maintained control over the final content.

Availability of Data and Material The survey materials and datasets generated and/or analyzed during the current study are not publicly available as they are the intellectual property of Adelphi Real World. All requests for access should be addressed directly to Jack Wright at jack.wright@adelphigroup.com.

Code Availability The codes used during the statistical analyses are available on reasonable request. All requests for access should be addressed directly to Jack Wright at jack.wright@adelphigroup.com.

Declarations

Conflict of Interest K. Ray Chaudhuri has received honoraria for lectures from AbbVie, Britannia, UCB, Zambon, Novartis, Boehringer Ingelheim, and Bial; has taken part in advisory boards for and acted as a consultant for AbbVie, UCB , GKC, Bial, Cynapsus, Lobsor, Stada, Medtronic, Zambon, Profile, Sunovion, Roche, Therevance, Scion, Britannia, Acadia, and 4D; and has received grants for investigator-initiated research from Britannia Pharmaceuticals, AbbVie, UCB, GKC, and Bial, and academic grants from EU, IMI EU, Horizon 2020, Parkinson's UK, NIHR, Parkinson's disease NMG, EU (Horizon 2020), Kirby Laing Foundation, NPF, MRC, and Wellcome Trust. Per Odin has received honoraria for lectures and advice from Britannia, Bial, Ever Pharma, Nordic Infucare, and Zambon, and has received honoraria for lectures and advice as well as research grants from AbbVie. Jean-Philippe Azulay, Susanna Lindvall, and J Josefa Domingos have no conflicts of interest that are directly relevant to the content of this article. Ali Alobaidi, Prasanna L. Kandukuri, Juan Carlos Parra, and Toru Yamazaki are employees of AbbVie and may own stocks/shares in the company. Vivek S. Chaudhari is a former employee of AbbVie Inc., currently employed by EMD Serono, Inc. and may hold AbbVie stock. Julia Oddsdottir is an employee of IQVIA, which received consultancy fees from AbbVie. Jack Wright is an employee of Adelphi Real World, a consulting company that was hired by AbbVie to perform analyses on the Adelphi Disease Specific Program database. Pablo Martinez-Martin has received honoraria from Bial, for participation in a course, and from the International Parkinson and Movement Disorder Society for activities during the International Congress 2023 and for directing the Clinical Outcome Assessment Program.

Ethics Approval Using a checkbox, patients provided informed consent to take part in the survey. Data were collected in such a way that patients and physicians could not be identified directly, and no personally identifiable data were collected. Physician and patient data were pseudo-anonymized. A code was assigned when data were collected.

Upon receipt by the study team, data were pseudo-anonymized again to mitigate against tracing them back to the individual. Data were aggregated before being shared with the researchers and/or for publication. The DSP follows all relevant market research guidelines and complies with the Health Insurance Portability and Accountability Act and equivalent EU European Pharmaceutical Marketing Research Association guidelines and because of the nature of the data, the collection and aggregation did not require ethics committee approval. The DSP and all questionnaires therein were granted an exemption following review by the Western Institutional Review Board (Puyallup, WA, USA) on 3 July, 2019 (AG8689).

Consent to Participate Respondents provided informed consent for use of their data; all data were aggregated and de-identified before receipt.

Consent for Publication Not applicable.

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