Parkinsonism and Related Disorders 68 (2019) 95–101

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

# Increases in institutionalization, healthcare resource utilization, and mortality risk associated with Parkinson disease psychosis: Retrospective cohort study

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ARTICLE INFO

*Keywords:*
Custodial care
Death
Parkinson disease
Psychosis

ABSTRACT

*Introduction:* Patients with Parkinson disease (PD) often develop psychosis (P). The association of PDP with death and long-term custodial care (CC) has not been well studied.

*Methods:* Medicare Parts A, B, and D data, 2007–2015, were used to define cohorts of PD and PDP patients. PD was defined by ≥ 2 ICD-9-CM codes (332.0x) at least 30, but no more than 365, days apart, and PDP by ≥ 2 codes for psychotic symptoms. Outcomes were CC use, defined as nursing home stays of > 100 consecutive days, and death. To compare the association of PDP with outcomes, PDP patients were matched to PD patients without psychosis.

*Results:* Within 1 year of PDP diagnosis, 12.1% of PDP patients used CC, versus 3.5% of non-PDP patients 1 year after the matching date; corresponding percentages at 5 years were 25.8% and 10.0%. Cumulative incidence curves for CC and for death differed significantly ($P < 0.0001$). PDP was associated with RRs of 3.38 (95% CI, 2.93–3.90) for CC and 1.34 (1.23–1.45) for death. Other factors associated with CC were age (3.57, 2.08–6.14, age ≥90 versus ≤70 years) and female sex (1.37, 1.18–1.58). Female sex was associated with a lower RR for death (0.76, 0.70–0.82). Health care utilization and costs were substantially higher for PDP than for non-PDP patients.

*Conclusion:* In PD patients, psychosis was associated with a more than 3-fold increased risk of CC and a nearly one-third increased risk of death. Women entered CC more often than men, likely because they lived longer in the setting of PD.

## 1. Introduction

Parkinson disease, a multisystem degenerative disorder affecting more than 6 million individuals worldwide [1], is often complicated by psychosis [2,3]. Parkinson disease psychosis (PDP) has profound implications for patients and their caregivers and often results in institutionalization of affected individuals [3]. PDP treatment is generally poor [4–7], as antipsychotic drugs can exacerbate Parkinson disease-related motor symptoms [8] and are associated with increased mortality.

Many epidemiologic questions about PDP are unanswered. Patterns of long-term institutionalization, known as custodial care (CC), in patients who experience an episode of PDP have not been fully characterized, and the association of PDP with CC and with death has not been quantified. We therefore undertook a retrospective study of patients with PDP using Medicare data. Using a billing claims-based strategy to identify patients with Parkinson disease and an episode of PDP, we determined CC use patterns, associations of PDP episodes with CC and death, and health care costs associated with PDP. Given the aging of the world's population [9] and the expected increase in numbers of individuals with Parkinson disease [10], understanding the potential implications of PDP could provide important information for

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https://doi.org/10.1016/j.parkreldis.2019.10.018
Received 22 July 2019; Received in revised form 9 September 2019; Accepted 18 October 2019

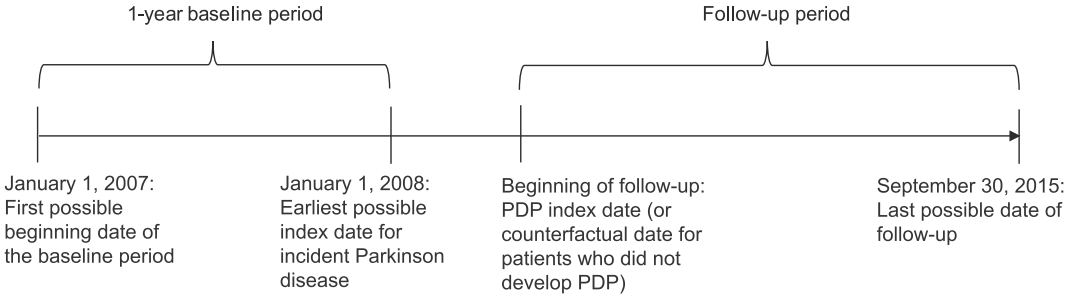


**Fig. 1.** Illustration of pre-CC and post-CC periods. CC, custodial care.

patients, providers, payers, and other health care stakeholders.

## 2. Materials and methods

### 2.1. Data sources

Data were sourced from the 2007–2015 20% Medicare random sample. Medicare health insurance consists of, among other things, Part A ("hospital insurance") coverage for care provided in the inpatient setting, skilled nursing facilities, hospice, or the home health care setting; Part B ("medical insurance") coverage for physician services (e.g., procedures, injections, and diagnostic tests) whether rendered in the inpatient or outpatient setting, and other outpatient care, medical supplies, or durable medical equipment (e.g., oxygen tanks and wheelchairs), preventive services, and some home health care; Part D offers the option to purchase prescription drug coverage (exercised by approximately 70% of Medicare beneficiaries as of 2014). Parts A, B, and D are available through traditional Medicare fee-for-service plans [11].

Medicare data included enrollment information, demographic characteristics, and medical claims from Parts A, B, and D. Medicare claims files contain information collected by Medicare to allow payment for health services provided to Medicare beneficiaries (primarily individuals aged 65 years or older) in the US and its territories. More information on use of Medicare data is available in the Supplementary Methods.

### 2.2. Study population and identification of Parkinson disease and PDP

The study population included patients aged 40 years or older who had Medicare fee-for-service coverage (encompassing Parts A and B, but with no health maintenance organization coverage) and who were included in the Medicare 20% random sample. Patients with presumed incident Parkinson disease were identified between 2008 and 2015, permitting a minimum of a 1-year look-back period (2007) to establish incidence of Parkinson disease. Patients were identified using two claims for primary/idiopathic Parkinson disease (International Classification of Diseases, Ninth Revision, Clinical Modification code 332.0x) [12,13] at least 30 days, but no more than 1 year, apart. Claims could be from inpatient or outpatient sources, and, if from an inpatient source, in any position. We excluded individuals with: (1) two or more codes at any time during the study period (before or after Parkinson disease diagnosis) for putative dementia etiologies more specific than Parkinson disease, or (2) one or more codes for presenile or senile dementia (290.1–290.3) after Parkinson disease diagnosis, or (3) one or more claims at any time for chronic psychiatric disease, or (4) one or more claims for alcohol-induced psychotic or delusional disorders before Parkinson disease diagnosis. Codes used for exclusions appears in Table S1.

To establish the presence of incident PDP among the patients with Parkinson disease, we used two or more codes more than 30 days apart for psychosis/delusions/hallucinations as listed in Table S2. We assumed that development of psychosis in patients with Parkinson disease could be attributed to the Parkinson disease. We further excluded individuals meeting the following criteria: (1) psychosis before the Parkinson disease date, (2) PDP in the year before the Parkinson disease diagnosis date, (3) age younger than 40 years on the PDP index date, (4) lack of Medicare Parts A and B coverage for at least 1 year before the PDP index date, or (5) CC stay (see below for CC definition) spanning the PDP index date, but no other CC stay thereafter. The PDP index date was the earliest diagnosis date of PDP, on or after the diagnosis of Parkinson disease, provided there was no evidence of PDP in the previous year. The earliest PDP index date was therefore January 1, 2008 (to permit a 1-year look-back period to establish incident psychosis).

### 2.3. Determination of use of custodial care

CC, identified from Medicare claims data based on a conceptual framework by the Centers for Medicare & Medicaid Services (CMS) [14] and a validation method using MarketScan data [15], was defined as an institutionalization stay of longer than 100 days. More details are provided in the Supplementary Methods.

### 2.4. Study design

A retrospective cohort design was used. The study period, including baseline and follow-up, comprised January 1, 2007, to September 30, 2015. Patients with and without PDP were followed for institutionalization in a CC setting and for death; end of follow-up occurred at death, loss of Medicare Parts A, B, or D eligibility, or the end of the study period. Specific details of the design are shown in the Supplementary Methods. The baseline period, used to define comorbid conditions and hospital and skilled nursing facility (SNF) stays, consisted of the 1-year period prior to the beginning of follow-up. Fig. 1 illustrates the study design.

### 2.5. Covariates

Comorbid conditions were defined by at least one inpatient, SNF, home health, or hospice claim or at least two outpatient, physician encounter, or durable medical equipment claims on different days during the 1-year baseline period. Comorbid conditions were the same as those listed in the Charlson Comorbidity Index [16] (Table 1).

### 2.6. Outcomes and cost calculations

Outcomes in the follow-up period included all-cause death, incidence of CC, health care utilization, and associated costs. Assessment of health care utilization and costs included inpatient, emergency department encounters or observation stays not resulting in formal hospitalization, other outpatient encounters, SNF admissions, use of home health/hospice services, physician visits, and Medicare Part D pharmacy medication fills.

**Table 1**
Baseline characteristics for incident Parkinson disease patients with and without psychosis.

| | Psychosis after Parkinson Disease Index Date | | *P* |
|---|---|---|---|
| | Yes | No | |
| | *n* (%) | *n* (%) | |
| Overall | 2778 (100) | 49,325 (100) | |
| Mean age (SD) | 80.0 (7.7) | 78.8 (8.2) | < 0.0001 |
| Age, years | | | |
| ≤ 70 | 370 (13.32) | 8835 (17.91) | |
| 71-75 | 452 (16.27) | 9040 (18.33) | |
| 76-80 | 611 (21.99) | 10,795 (21.89) | |
| 81-85 | 706 (25.41) | 10,714 (21.72) | |
| 86-90 | 478 (17.21) | 7047 (14.29) | |
| > 90 | 161 (5.80) | 2894 (5.87) | |
| Sex | | | < 0.0001 |
| Male | 1442 (51.91) | 27,680 (56.12) | |
| Female | 1336 (48.09) | 21,645 (43.88) | |
| Race | | | < 0.0001 |
| White | 2566 (92.37) | 44,206 (89.62) | |
| Black | 116 (4.18) | 2450 (4.97) | |
| Other | 96 (3.46) | 2669 (5.41) | |
| Comorbid conditions | | | |
| Myocardial infarction | 145 (5.22) | 2379 (4.82) | 0.3436 |
| Congestive heart failure | 435 (15.66) | 7631 (15.47) | 0.7899 |
| Peripheral vascular disease | 427 (15.37) | 7361 (14.92) | 0.5200 |
| Cerebrovascular disease | 485 (17.46) | 8102 (16.43) | 0.1534 |
| Dementia[a] | 261 (9.40) | 3447 (6.99) | < 0.0001 |
| Chronic pulmonary disease | 525 (18.90) | 9389 (19.03) | 0.8585 |
| Rheumatologic disease | 102 (3.67) | 1702 (3.45) | 0.5351 |
| Peptic ulcer disease | 31 (1.12) | 507 (1.03) | 0.6552 |
| Mild liver disease | 50 (1.80) | 937 (1.90) | 0.7074 |
| Diabetes without chronic complication | 765 (27.54) | 14,026 (28.44) | 0.3070 |
| Diabetes with chronic complication | 250 (9.00) | 4658 (9.44) | 0.4355 |
| Hemiplegia or paraplegia | 55 (1.98) | 910 (1.84) | 0.6078 |
| Renal disease | 365 (13.14) | 6040 (12.25) | 0.1628 |
| Any malignancy | 300 (10.80) | 5904 (11.97) | 0.0638 |
| Moderate or severe liver disease | [b] | 111 (0.23) | 0.2899 |
| Metastatic solid tumor | 19 (0.68) | 539 (1.09) | 0.0417 |
| AIDS HIV | [b] | 19 (0.04) | 0.3008 |
| *n* of comorbid conditions | | | 0.8327 |
| 0 | 936 (33.69) | 16,813 (34.09) | |
| 1 | 727 (26.17) | 13,050 (26.46) | |
| 2-3 | 773 (27.83) | 13,656 (27.69) | |
| 4-11 | 342 (12.31) | 5806 (11.77) | |
| Part D coverage | 1437 (51.73) | 25,319 (51.33) | 0.6838 |

SD, standard deviation.
[a] Represents a preexisting claim for dementia prior to diagnosis of Parkinson disease.
[b] Number is suppressed if patient count is less than 11.

### 2.7. Statistical analysis

Descriptive statistics (counts and percentages) were used to characterize patients with and without incident PDP. We compared differences in baseline characteristics between PDP and non-PDP patients using the chi-square test for categorical variables and the *t*-test for continuous variables.

To determine the association of PDP with the outcomes of interest (CC and, separately, death), we undertook direct matching, without replacement, on the basis of age (≤1 year difference between PDP and non-PDP patients), sex, race, number of selected comorbid conditions, status of Part D coverage at baseline (yes/no), and index year of PDP. For each Parkinson disease patient who developed PDP, we selected four who did not and established a "counterfactual" PDP date, that is, a date on which a Parkinson disease patient could have developed PDP but had not. (Of note, patients who were already in CC when they were diagnosed with PDP were excluded, as they could not be considered at future risk of this outcome.) We then followed patients from PDP index date for outcomes of interests. Cumulative incidence of outcomes was assessed using the Kaplan-Meier method. Cox proportional hazard regression was used to assess the association of PDP with outcomes, adjusting for demographic and baseline comorbid conditions. Because there is a theoretical concern about correlation between matched pairs, and because SAS software cannot allow for adjustment of correlation in the Cox proportional hazards regression setting, we conducted the analysis using two additional modeling approaches: Poisson regression with independent assumptions and Generalized Estimating Equation (GEE) modeling adjusting for correlation within matched pairs. The latter two models yielded very similar estimates, demonstrating that correlation was not a threat to the independence assumptions utilized by the Cox model. We henceforth report hazard ratios from the Cox models.

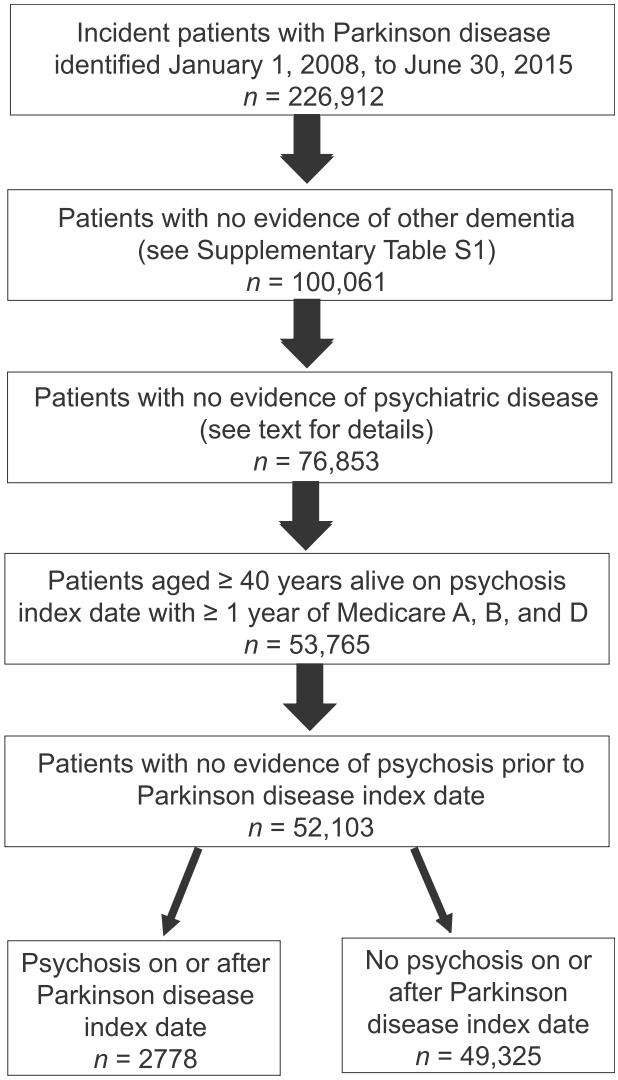


**Fig. 2.** Cohort selection.

## 3. Results

A total of 226,912 patients with qualifying Parkinson disease claims between 2008 and 2015 were identified (Fig. 2). After applying age- and Medicare-related criteria, 53,765 individuals remained. After excluding those with evidence of preexisting (prevalent) psychosis, 52,103 remained, of whom 2778 developed new (incident) psychosis

**Table 2**
Characteristics of custodial care use in Parkinson disease patients with and without psychosis.

| | PDP Patients | Non-PDP Patients |
|---|---|---|
| *n* overall | 1699 | 6796 |
| Days of follow-up, all patients | | |
| Mean (SD) | 788.78 (569.45) | 801.60 (599.71) |
| Median | 659 | 658 |
| *n* (%) with CC use during follow-up | 333 (19.60) | 442 (6.50) |
| Days of follow-up, CC patients | | |
| Mean (SD) | 999.64 (557.05) | 1055.35 (594.94) |
| Median | 943 | 926.5 |
| *n* of CC stays during follow-up, CC patients | | |
| Mean (SD) | 1.24 (0.59) | 1.22 (0.54) |
| Median | 1 | 1 |
| Days to first CC stay, CC patients | | |
| Mean (SD) | 415.93 (450.89) | 524.97 (493.32) |
| Median | 266 | 343.5 |
| Days of CC stay, CC patients | | |
| Mean (SD) | 422.49 (346.33) | 395.16 (330.16) |
| Median | 321 | 277 |

CC, custodial care; PDP, Parkinson disease psychosis; SD, standard deviation.

and 49,325 did not, and were therefore available for matching.

Characteristics of the cohort are shown in Table 1. In general, Parkinson disease patients who developed PDP were more likely to be older (by approximately 1 year), to be female, and to be white. Incident PDP patients ($n = 1699$) were successfully matched 1:4 with Parkinson disease patients who did not develop PDP to create the matched cohort; results of the matching process, shown in Table S3, demonstrated that, as designed, the two groups were highly similar.

Characteristics of CC use, by presence/absence of PDP, are shown in Table 2. Of Parkinson disease patients without psychosis, 6.5% required CC compared with 19.6% of those with PDP. Follow-up duration for CC users was similar between the groups. However, mean time to first CC stay was shorter (416 days) for PDP patients than for non-PDP patients (525 days), and mean duration of CC stay was longer for PDP patients (422 days) than for non-PDP patients (395 days).

The cumulative incidence of CC for Parkinson disease patients with and without PDP (i.e., the matched cohort), with death considered as a competing risk, is shown in Fig. 3A. The curves differed significantly ($P < 0.0001$). Within 1 year of PDP diagnosis, 12.1% of PDP patients required CC; within 1 year of the corresponding counterfactual date, 3.5% of non-PDP patients required CC. Corresponding percentages at 3 years were 21.4% and 7.1%, respectively; at 5 years, 25.8% and 10.0%; and at 8 years, 28.3% and 12.5%. Precise values for each year are shown in Table S4. Cumulative incidence of death is shown in Fig. 3B. The curves again differed significantly ($P < 0.0001$), but the differences were smaller than differences for CC use. Percentages of death at varying time points for PDP and non-PDP patients are also shown in Table S4.

Factors associated with CC and, separately, death, are shown in Table 3 for the matched cohort. PDP was associated with a hazard ratio (HR) of 3.38 (95% confidence interval, 2.93–3.90) for CC. The HRs generated from the two alternative approaches, the traditional Poisson model and the GEE Poisson model, were 3.44 (2.98–3.98) and 3.86 (3.24–4.60), respectively (not shown). Other factors associated with CC were age (3.57, 2.08–6.14 for age ≥ 90 years compared with the referent group aged ≤ 70 years) and female sex (1.37, 1.18–1.58), with a trend for non-white race (1.62, 0.52–5.08).

For the outcome of death, PDP was associated with an HR of 1.34 (1.23–1.45) using the Cox model; HRs for the traditional Poisson and Poisson GEE models were 1.33 (1.23–1.45) and 1.38 (1.21–1.57), respectively (not shown). Older age was associated with death, as would be expected, but female sex was associated with a lower HR for death (0.76, 0.70–0.82).

Annualized all-cause health care resource utilization in Parkinson disease patients during follow-up is shown in Table 4 for patients with and without PDP (matched cohort). Inpatient admissions, emergency department encounters/observation stays, outpatient visits, SNF use, and use of home health/hospice services were nearly double for PDP compared with non-PDP patients. Physician visits were somewhat higher, and Part D prescription drug fills were approximately one-and-a-half times higher for PDP than for non-PDP patients.

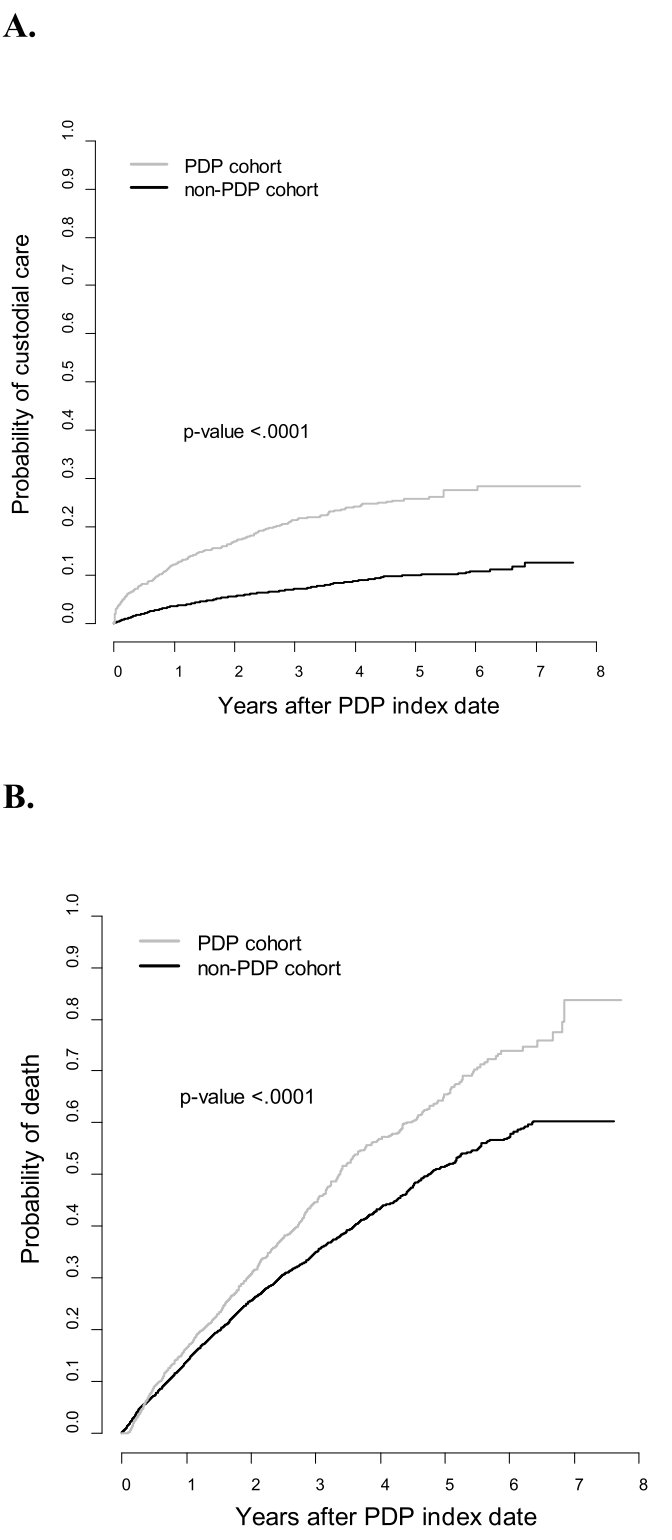


**Fig. 3.** Cumulative incidence of custodial care (panel A, death as a competing risk) and death (panel B) among incident PDP patients. CC, custodial care; PDP, Parkinson disease psychosis.

**Table 3**
Adjusted hazard ratios of custodial care and death during follow-up among patients with incident Parkinson disease.

| | Custodial Care | | Death | |
|---|---|---|---|---|
| | HR (95% CI) | *P* | HR (95% CI) | *P* |
| PDP | | | | |
| No | 1.00 (ref) | | 1.00 (ref) | |
| Yes | 3.38 (2.93–3.90) | < 0.0001 | 1.34 (1.23–1.45) | < 0.0001 |
| Age- years | | | | |
| ≤ 70 | 1.00 (ref) | | 1.00 (ref) | |
| 71-75 | 1.75 (1.20–2.55) | 0.0037 | 1.52 (1.25–1.86) | < 0.0001 |
| 76-80 | 2.39 (1.67–3.42) | < 0.0001 | 2.69 (2.23–3.24) | < 0.0001 |
| 81-85 | 3.45 (2.43–4.90) | < 0.0001 | 3.67 (3.06–4.41) | < 0.0001 |
| 86-90 | 5.77 (4.05–8.23) | < 0.0001 | 5.05 (4.19–6.09) | < 0.0001 |
| > 90 | 3.57 (2.08–6.14) | < 0.0001 | 7.52 (5.90–9.58) | < 0.0001 |
| Sex | | | | |
| Male | 1.00 (ref) | | 1.00 (ref) | |
| Female | 1.37 (1.18–1.58) | < 0.0001 | 0.76 (0.70–0.82) | < 0.0001 |
| Race | | | | |
| White | 1.00 (ref) | | 1.00 (ref) | |
| Non-white | 1.62 (0.52–5.08) | 0.4057 | 0.69 (0.29–1.66) | 0.4054 |
| Comorbid conditions | | | | |
| Myocardial infarction | 1.11 (0.74–1.66) | 0.619 | 0.87 (0.70–1.08) | 0.2067 |
| Congestive heart failure | 1.20 (0.95–1.50) | 0.1189 | 1.28 (1.14–1.43) | < 0.0001 |
| Peripheral vascular disease | 1.22 (0.99–1.50) | 0.0626 | 1.08 (0.97–1.21) | 0.1609 |
| Cerebrovascular disease | 0.95 (0.78–1.17) | 0.6589 | 1.04 (0.94–1.16) | 0.4111 |
| Dementia[a] | 1.91 (1.47–2.48) | < 0.0001 | 1.87 (1.63–2.14) | < 0.0001 |
| Chronic pulmonary disease | 0.87 (0.71–1.08) | 0.2143 | 1.16 (1.05–1.29) | 0.0035 |
| Rheumatologic disease | 1.35 (0.92–1.97) | 0.1261 | 1.23 (1.00–1.52) | 0.0473 |
| Peptic ulcer disease | 1.33 (0.63–2.80) | 0.4567 | 1.17 (0.79–1.72) | 0.4352 |
| Mild liver disease | 0.71 (0.33–1.53) | 0.3808 | 0.96 (0.67–1.38) | 0.8288 |
| Diabetes without chronic complication | 1.05 (0.87–1.27) | 0.5937 | 0.99 (0.90–1.09) | 0.8725 |
| Diabetes with chronic complication | 1.15 (0.83–1.59) | 0.4109 | 1.15 (0.97–1.36) | 0.1091 |
| Hemiplegia or paraplegia | 1.47 (0.83–2.62) | 0.188 | 1.42 (1.01–1.98) | 0.0426 |
| Renal disease | 1.04 (0.80–1.35) | 0.787 | 1.15 (1.01–1.31) | 0.0375 |
| Any malignancy | 0.70 (0.53–0.93) | 0.0128 | 1.00 (0.89–1.13) | 0.9933 |
| Moderate or severe liver disease | 2.28 (0.30–17.35) | 0.4261 | 2.60 (0.95–7.10) | 0.0628 |
| Metastatic solid tumor | 4.87 (2.22–10.70) | < 0.0001 | 3.28 (2.24–4.79) | < 0.0001 |

[a] Represents a preexisting claim for dementia prior to diagnosis of Parkinson disease.

**Table 4**
Annualized all-cause health care resource utilization for PDP and non-PDP cohorts.

| Follow-up | Weighted Mean of Claims per Patient per Year | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *n* of Patients | | Inpatient | | ED/OB | | Outpatient[a] | | SNF | | HH/HS | | Physician Visits | | Part D Fills | |
| | PDP | Non-PDP | PDP | Non-PDP | PDP | Non-PDP | PDP | Non-PDP | PDP | Non-PDP | PDP | Non-PDP | PDP | Non-PDP | PDP | Non-PDP |
| 1-year baseline | 1699 | 6796 | 0.8 | 0.4 | 1.0 | 0.6 | 6.3 | 4.8 | 0.4 | 0.2 | 0.7 | 0.6 | 25.2 | 22.3 | 29.5 | 25.3 |
| Year 1 | 1699 | 6793 | 1.0 | 0.5 | 1.2 | 0.7 | 7.5 | 5.0 | 1.2 | 0.3 | 1.4 | 0.8 | 30.2 | 23.0 | 36.5 | 27.9 |
| Year 2 | 1211 | 4859 | 0.7 | 0.5 | 1.0 | 0.6 | 7.1 | 4.9 | 0.7 | 0.3 | 1.1 | 0.8 | 25.0 | 22.5 | 41.4 | 29.9 |
| Year 3 | 775 | 3100 | 0.7 | 0.5 | 1.1 | 0.7 | 6.7 | 5.0 | 0.8 | 0.3 | 1.2 | 0.8 | 25.1 | 22.3 | 45.9 | 31.3 |
| Year 4 | 458 | 1923 | 0.6 | 0.5 | 1.1 | 0.7 | 6.9 | 5.1 | 0.7 | 0.3 | 1.2 | 0.9 | 24.7 | 22.0 | 47.4 | 32.9 |
| Year 5 | 230 | 1058 | 0.8 | 0.5 | 1.2 | 0.8 | 7.3 | 5.1 | 0.7 | 0.4 | 1.4 | 1.0 | 25.7 | 22.2 | 49.1 | 36.0 |
| Year ≥6 | 109 | 497 | 0.9 | 0.5 | 1.5 | 0.7 | 10.2 | 5.3 | 1.1 | 0.4 | 1.8 | 0.9 | 26.7 | 21.4 | 53.7 | 37.1 |

ED, emergency department; HH, home health; HS, hospice; OB, observation; PD, Parkinson disease; PDP, Parkinson disease psychosis; SNF, skilled nursing facility.
[a] Non-ED/OB.

Total costs over time are shown in Table 5 for the matched cohort. Total Medicare costs, and costs related to CC were nearly double for PDP patients compared with non-PDP patients. For example, overall Medicare, long-term care, and total costs for PDP vs. non-PDP patients in year 1 were $41,690 vs. $21,633, $5378 vs. $1867, and $47,068 vs. $23,500, respectively. Analogous costs for year 6 and beyond were $36,952 vs. $19,326, $14,695 vs. $5475, and $51,647 vs. $24,801, respectively.

## 4. Discussion

In this study, we found that development of an episode of PDP was associated with a substantially increased risk of both CC use and death. Indeed, within 5 years of PDP diagnosis, one in four PDP patients required CC, compared with only one in ten patients without PDP who were otherwise similar. Health care utilization and costs were substantially higher for PDP patients than for patients who did not develop psychosis; some of the increased cost was due to CC itself, but much was due to other non-CC-related costs. Overall, our study shows how development of PDP in patients with Parkinson disease is associated with a host of adverse clinical, resource-intensive, and costly outcomes.

Given that PDP is likely to become a greater challenge for industrialized societies in the coming decade as the population ages and Parkinson disease becomes more prevalent [10], an increased epidemiological understanding of the implications of PDP is important. The present report supplements other studies of PDP [12] but considerably

**Table 5**
Annualized all-cause costs in 2015 US dollars for PDP and non PDP cohorts.

| Follow-up | Weighted Mean of Cost ($) per Patient per Year | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *n* of Patients | | Inpatient | | ED/OB | | Outpatient[a] | | SNF | | HH/HS | |
| | PDP | Non-PDP | PDP | Non-PDP | PDP | Non-PDP | PDP | Non-PDP | PDP | Non-PDP | PDP | Non-PDP |
| 1-year baseline | 1699 | 6796 | 6741 | 4837 | 832 | 479 | 2189 | 1753 | 2854 | 1784 | 2128 | 1922 |
| Year 1 | 1699 | 6793 | 14,258 | 6314 | 1007 | 563 | 2903 | 1933 | 9520 | 2737 | 4866 | 2843 |
| Year 2 | 1211 | 4859 | 8420 | 5543 | 852 | 524 | 2844 | 1883 | 4651 | 2376 | 3703 | 2798 |
| Year 3 | 775 | 3100 | 7266 | 5748 | 902 | 566 | 2895 | 1970 | 5070 | 2272 | 3867 | 2676 |
| Year 4 | 458 | 1923 | 6579 | 5061 | 933 | 570 | 2671 | 1789 | 4820 | 2559 | 3915 | 2883 |
| Year 5 | 230 | 1058 | 8839 | 5093 | 815 | 660 | 2946 | 1913 | 5566 | 2955 | 4271 | 3192 |
| Year ≥ 6 | 109 | 497 | 11,411 | 4634 | 1389 | 528 | 3793 | 1709 | 6120 | 2978 | 5550 | 3112 |
| | *n* of Patients | | PD Visits/DME | | PD Fills | | Total Medicare | | LTC[b] | | Total | |
| | PDP | Non-PDP | PDP | Non-PDP | PDP | Non-PDP | PDP | Non-PDP | PDP | Non-PDP | PDP | Non-PDP |
| 1-year baseline | 1699 | 6796 | 5608 | 4779 | 2111 | 1834 | 22,463 | 17,387 | 1512 | 1055 | 23,975 | 18,442 |
| Year 1 | 1699 | 6793 | 6720 | 5198 | 2416 | 2043 | 41,690 | 21,633 | 5378 | 1867 | 47,068 | 23,500 |
| Year 2 | 1211 | 4859 | 5238 | 4903 | 2669 | 2172 | 28,377 | 20,200 | 8661 | 2986 | 37,038 | 23,186 |
| Year 3 | 775 | 3100 | 5284 | 4929 | 2830 | 2311 | 28,114 | 20,472 | 10,170 | 3282 | 38,284 | 23,754 |
| Year 4 | 458 | 1923 | 4628 | 4610 | 2629 | 2238 | 26,175 | 19,710 | 12,201 | 4479 | 38,375 | 24,189 |
| Year 5 | 230 | 1058 | 4937 | 4487 | 2798 | 2420 | 30,172 | 20,721 | 13,738 | 5446 | 43,910 | 26,166 |
| Year ≥ 6 | 109 | 497 | 5556 | 4021 | 3134 | 2344 | 36,952 | 19,326 | 14,695 | 5475 | 51,647 | 24,801 |

DME, durable medical equipment; ED, emergency department; HH, home health; HS, hospice; LTC, long-term care; OB, observation; PD, Parkinson disease; PDP, Parkinson disease psychosis; SNF, skilled nursing facility.

[a] Non-ED/OB.

[b] Daily LTC nursing home costs varied from $155.5 to $771.0 per day, average of daily semi-private and daily private room. Source: http://skloff.com/cost-of-long-term-care-by-state-2015/.

expands previous work. Our most important findings were that development of PDP was associated with a more than tripled risk of CC and an increase in the risk of death by about one-third. Juxtaposing these risks is essential to the understanding of PDP-related health outcomes: high mortality rates in this population likely affected the association of risk factors with CC use. For example, older age was strongly associated with both death and CC, which is not unexpected. However, the pattern for sex was more complex; after adjustment for other factors, women were more likely than men to require CC, but this was likely because men, who do not live as long, on average, as women, were substantially more likely to die with PDP before they needed CC. Although there may have been a trend for an association of non-white race with CC, due to real-world disparities in ascertainment of Parkinson disease in black, relative to white, patients we were unable to make informed conclusions about this.

In addition to being more likely to use CC, patients with PDP entered CC somewhat more quickly, and remained in CC somewhat longer, than patients without PDP. Given the association we found between development of PDP and use of CC, it is unsurprising that PDP was associated with increased health care utilization and costs. Increased CC use by PDP, relative to non-PDP, patients, was partially but not wholly responsible; while CC is a major cost driver in dementia in general irrespective of psychosis [17], PDP was associated with increased costs even for patients who did not require CC. By providing an estimate of costs associated with CC in patients with PDP, our study provides the groundwork for future cost-benefit analyses, should future drugs demonstrate utility in preventing or forestalling CC in patients with psychosis [18,19].

A prior claim for dementia was associated with both death and use of CC. While an episode of psychosis is a manifestation of Parkinson disease that likely occurs primarily in Parkinson disease patients with dementia, the association of a preexisting dementia claim (that is, a dementia claim appearing prior to the establishment of Parkinson disease) likely signifies that such patients had more advanced Parkinson disease than those without a dementia claim. However, even after adjusting for this presumed marker of Parkinson disease severity, development of psychosis was strongly associated with the adverse outcomes of interest.

Our study has several important limitations. First, as with any observational study, causality cannot be inferred. Second, because our approach to identifying Parkinson disease and PDP has not been validated, such as by chart review, under-ascertainment of these conditions is possible. This is particularly true for black, as opposed to white, patients, who likely have higher rates of undiagnosed Parkinson disease and, therefore, PDP. While we attempted to study individuals whose psychosis was plausibly related to Parkinson disease, we used an approach that heavily favored specificity; some degree of misclassification is nevertheless likely. Third, we assumed that development of psychosis in patients with Parkinson disease was attributable to the Parkinson disease itself; this assumption is not definitively testable using Medicare data and, given that psychosis can be caused by many factors, may have led to overestimation of the putative effects of PDP. Additionally, our definition of CC was drawn from previous work designed to identify individuals likely to be receiving care for the indefinite future, but we found that some patients, despite being in non-hospitalized care for longer than 100 days, returned to noninstitutionalized settings. We also cannot make informed conclusions about the role of medications in this disorder, as our investigation was not designed as a comparative effectiveness study. Finally, we studied only US patients with Medicare. While Medicare, which provides insurance coverage for more than 50 million Americans (primarily elderly) [11], is an entitlement for individuals aged 65 years or older, some older individuals use primarily private health insurance, and our results cannot necessarily be generalized to them.

In conclusion, about one in four patients who experiences a PDP episode requires CC within 5 years, a rate substantially higher than for patients who did not develop PDP. A PDP episode was also associated with a significantly increased risk of death. Women were more likely to use CC than men, but less likely to die. Health care use and associated costs were substantially higher for PDP than for non-PDP patients, some of which was due to the need for CC. Further study of PDP is required.

## Declaration of competing interest

James B. Wetmore, Suying Li, Heng Yan, Yi Peng, and David T. Gilbertson are employed by the Chronic Disease Research Group, which receives research funding from ACADIA. Dr. Wetmore has served on *ad hoc* advisory boards for Amgen and Rockwell Medical. Dr. Gilbertson has provided statistical consulting for DaVita Clinical Research. Nazia Rashid and Andrew Shim are employees of ACADIA Pharmaceuticals Inc.

## Acknowledgments

This study was supported by a research grant from ACADIA Pharmaceuticals Inc., San Diego, California. The research protocol was approved by the institutional review board at Hennepin Healthcare Systems. A data use agreement between the Hennepin Healthcare Research Institute and the Centers for Medicare & Medicaid Services was in place.

The authors thank Chronic Disease Research Group colleagues Anne Shaw for manuscript preparation and Nan Booth, MSW, MPH, ELS, for manuscript editing.

## Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.parkreldis.2019.10.018.

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