RESEARCH ARTICLE

Mortality from Parkinson's Disease: A Population-Based Prospective Study (NEDICES)

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ABSTRACT: Most studies of mortality in Parkinson's disease have been clinical studies, yielding results that are not representative of the general population. We assessed the risk of mortality from Parkinson's disease in the Neurological Disorders in Central Spain (NEDICES) study, a prospective population-based study in which Parkinson's disease patients who were not ascertained through medical practitioners were also included. The cohort consisted of 5262 elderly subjects (mean baseline age, 73.0 years), including 81 with Parkinson's disease at baseline (1994–1995). Thirteen-year mortality was assessed. Two thousand seven hundred and one of 5262 subjects (51.3%) died over a median follow-up of 12.0 years (range, 0.04–14.8 years), including 66 of 81 subjects (81.5%) with Parkinson's disease at baseline and 2635 of 5181 subjects (50.8%) without Parkinson's disease at baseline. In an unadjusted Cox model, the hazard ratio of mortality was increased in subjects with Parkinson's disease (hazard ratio, 2.29; 95% confidence interval, 1.80–2.93; $P < .001$) versus subjects without Parkinson's disease (reference group). In a Cox model that adjusted for a variety of demographic factors and comorbidities, the risk of mortality remained elevated in subjects with Parkinson's disease (hazard ratio, 1.75; 95% CI, 1.32–2.31, $P < .001$). In additional Cox models, Parkinson's disease patients with dementia had particularly high risks of mortality (adjusted hazard ratio, 2.62; 95% CI, 1.40–4.90; $P < .001$). In this prospective population-based study, Parkinson's disease was an independent predictor of mortality in the elderly. Parkinson's disease patients with dementia had particularly high risks of mortality.

Key Words: elderly; epidemiology; mortality; Parkinson's disease

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Funding agencies: This work was supported by FIS 93/0773 and Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), Spain.
Relevant conflicts of interest/financial disclosures: Julián Benito-León is supported by NIH R01 NS039422 from the National Institutes of Health (Bethesda, MD). Elan Louis is supported by R01 NS042859 and R01 NS039422 from the National Institutes of Health (Bethesda, MD). Félix Bermejo-Pareja is supported by NIH R01 NS039422 from the National Institutes of Health (Bethesda, MD).
Full financial disclosures and author roles may be found in the online version of this article.

Received: 5 April 2011; **Revised:** 5 July 2011; **Accepted:** 21 July 2011
Published online 13 September 2011 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mds.23921

During the past 20 years, 30 surveys worldwide have produced a variety of statistics on mortality in Parkinson's disease (PD),[1–30] and an increased risk of mortality is the norm. Yet most of the current data are derived from clinical studies[2,3,5,6,8,10,11,14–18,22,24,25,27–30] rather than population-based studies.[1,4,7,9,12,13,19–21,23,26] Even among the latter,[1,4,7,9,12,13,19–21,23,26] patients were either referred to the studies by practitioners or were ascertained through a medical records linkage system.[1,4,7,9,13,19,20,21] There are only 3 population-based studies in which patients were ascertained directly from the population.[12,23,26] The mortality risk

associated with PD from these 3 studies ranged from 1.8 to 2.3.[12,23,26] Thus, with few exceptions,[12,23,26] the prevailing studies would have excluded patients who do not seek medical advice, thereby selecting patients with more severe forms of the disease and a higher risk of mortality. The scarcity of population-based studies of mortality in PD patients motivated us to examine mortality at 13 years from PD in the Neurological Disorders in Central Spain (NEDICES) study, a prospective population-based study in which all subjects were assessed for PD irrespective of their medical care or practitioner referrals.[31,32]

Patients and Methods

Study Population

Data for these analyses were derived from the NEDICES study, a longitudinal population-based survey of the prevalence, incidence, and determinants of major age-associated conditions of the elderly, including PD, essential tremor, stroke, and dementia.[31–41] Detailed accounts of the study population and sampling methods have been published.[38–41] The study population was composed of elderly subjects $\geq$ 65 years old living in 3 communities in central Spain (Las Margaritas, Lista, and Arévalo). The registered study population was 6395, but 481 people were ineligible (census issues, address errors, or death), leaving 5914 eligible subjects, of whom 5278 were enrolled. All procedures were approved by the Ethical Standards Committees on Human Experimentation at University Hospitals "12 de Octubre" (Madrid) and "La Princesa" (Madrid). Written (signed) informed consent was obtained from all subjects on enrollment.

Study Design

Detailed accounts of the study assessments have been published.[38–41] Face-to-face evaluations were performed at baseline (1994–1995). During this face-to-face evaluation, data were collected by questionnaire on demographics, current medications, medical conditions (eg, diabetes mellitus, hypertension, heart disease), smoking (ever vs never), and consumption of ethanol (ever at least once per week vs never). The presence of a history of hypertension or diabetes was assessed by asking subjects whether a physician had given them a diagnosis of either of these conditions or whether they were receiving antihypertensive or antidiabetic drugs. Most important for this study, the questionnaire included 3 questions to screen for parkinsonism (ie, 1 each about previous diagnosis of PD, presence of tremor, and presence of bradykinesia).[31,32] Subjects screened positive for parkinsonism if they responded positively to 1 or more of these 3 questions. To assess the performance of these screening questions, a random sample of approximately 4% of those who had screened negative was selected and contacted (n = 205). Of the 205 subjects who were contacted, 183 were successfully scheduled for an examination by a senior neurologist who routinely evaluates patients with movement disorders (J.O. [see acknowledgments]). Parkinsonian signs were assessed using the motor portion of the Unified Parkinson's Disease Rating Scale (UPDRS).[42] None of the 183 subjects (0%) was found to have PD (see diagnostic criteria below), indicating that use of these screening questions was likely to yield few false negatives.[38] We assessed depressive symptoms by self-report, using a single screening question ("Do you suffer from depression?"). This same approach has similarly been utilized in other previous studies of depression.[43] We also assessed the use of antidepressant medications, a marker that may be less prone to biases than a simple screening question.

A short form of the study questionnaire was mailed to subjects who refused or were unavailable for face-to-face screening. This shorter questionnaire assessed demographic characteristics, medications, and medical conditions including several neurological disorders (essential tremor, stroke, dementia, and parkinsonism).

PD Cases and Controls

Persons who screened positive for PD underwent a neurological examination[31,32] that comprised a general neurological examination and the motor portion of the Unified Parkinson's Disease Rating Scale (UPDRS).[42] The neurological examination was performed by 1 of 8 senior neurologists who met at the inception of the study to establish standardized methods to perform and interpret the examination (J.B.-L., F.B.-P., and see acknowledgments: A.B., A.M.-S., J.D.-G., J.O., J.P., and J.P.-E.). For subjects who could not be examined, medical records were obtained from their general practitioners, from in-patient hospitalizations, and from neurological specialists (if they had visited one). Parkinsonism was diagnosed when at least 2 cardinal signs (resting tremor, rigidity, bradykinesia, and impaired gait/postural reflexes) were present.[31,32] PD was diagnosed in patients without secondary causes of parkinsonism or atypical features. A Hoehn and Yahr stage was assigned to each case.[44] For the diagnosis of dementia, we applied the Diagnostic and Statistical Manual of Mental Disorders (DSM)–IV criteria.[45]

Mortality Assessment

Follow-up data on death were collected until May 1, 2007. Date of death was obtained from the National Population Register of Spain (Instituto Nacional de Estadística). In Spain, all deceased individuals receive a death certificate, completed by a

TABLE 1. Baseline demographic and clinical characteristics of subjects with and without Parkinson's disease

Characteristics at baseline evaluation	Subjects with PD (n = 81)	Subjects without PD (n = 5181)	*P* value
Age (y)	77.0 ± 5.5 (77.0)	74.3 ± 7.0 (73.0)	< .001
Male sex	33 (40.7%)	2198 (42.4%)	.761
Geographical area			
Arévalo county (rural area)	35 (43.2%)	1889 (36.5%)	.360
Las Margaritas (blue collar area)	22 (27.2%)	1752 (33.8%)	
Lista (white collar area)	24 (29.6%)	1540 (29.7%)	
Education[a]			
Illiterate	15 (18.8%)	693 (13.5%)	.580
Can read and write	29 (36.3%)	2059 (40.1%)	
Primary studies	26 (32.5%)	1687 (32.8%)	
≥Secondary studies	10 (12.5%)	697 (13.6%)	
Self-reported ever smoker[a]	24 (34.8%)	1578 (39.0%)	.477
Self-reported ever drinker[a]	31 (44.9%)	2204 (54.5%)	.112
Self-reported hypertension[a]	47 (58.8%)	2516 (51.0%)	.167
Self-reported diabetes mellitus[a]	14 (17.7%)	825 (16.8%)	.828
Self-reported chronic obstructive pulmonary disease[a]	10 (12.7%)	771 (16.0%)	.422
Self-reported osteoarthritis[a]	44 (56.4%)	2,935 (60.9%)	.423
Self-reported heart disease[a]	2 (2.6%)	505 (10.2%)	.03
Self-reported depressive symptoms or antidepressant use[a]	37 (47.4%)	1143 (25.4%)	< .001
Dementia	13 (16.0%)	293 (5.7%)	< .001
Stroke	6 (7.4%)	249 (4.8%)	.279
Number of medications[a]	3.1 ± 1.9 (3.0)	2.3 ± 1.8 (2.0)	< .001

Mean ± SD (median) is given for age and number of medications. The Mann–Whitney test was used for comparison of continuous data and the χ^2 test for proportions.
[a]n < 5262 because of missing data.

doctor, at the time of death. The certificate is then sent to the local police authority in the municipality where the person had been living, and the information is collected in the National Register. Cause of death (using the International Classification of Diseases ICD], 9th revision; http://www.cdc.gov/nchs/icd/icd9.htm) was classified into 7 main categories: PD, dementia, cerebrovascular disorders, cardiovascular disorders (pulmonary embolism, congestive heart failure, myocardial infarction, heart or aortic rupture, and asystole), respiratory diseases, cancer, and other causes (infections, trauma, genitourinary or gastrointestinal disorders).

Data Analyses

Statistical analyses were performed in SPSS version 18.0 (SPSS, Inc., Chicago, IL). All *P* values were 2 tailed, and we considered $P < .05$ as significant. Characteristics of subjects were compared using chi-square or Fisher's exact tests. If continuous variables were not normally distributed, Mann–Whitney and Kruskal–Wallis tests were used.

We used Cox proportional-hazards models to estimate hazard ratios (HRs) for mortality; this also generated 95% confidence intervals (CIs). The time variable was the years from the date of the first evaluation (1994 to 1995) to either (1) May 1, 2007, in living subjects or (2) the date of death in subjects who had died prior to May 1, 2007.

In the Cox proportional hazards analyses, we estimated the risks of mortality in subjects with baseline PD compared with the reference group (subjects without PD at baseline). In each analysis, we began with an unadjusted model. Then, in adjusted models, we first considered baseline variables that were associated with both baseline PD and death (model 1—more restrictive criteria for confounding) and then considered baseline variables that were associated with either baseline PD or death (model 2—less restrictive criteria for confounding).

Kaplan–Meier survival curves for subjects with PD versus controls were assessed; the log-rank test was used to compare the differences between the 2 curves.

Results

Beginning in January 1994, letters explaining the survey and inviting participation were mailed to 6395 subjects. Of these, 5914 subjects were deemed eligible for screening, and 5278 of 5914 subjects (89.2%) were screened. Of the 636 subjects who were not screened, 292 (45.9%) declined, 292 (45.9%) could not be located because of an address change, and 52 (8.2%) had died. Of the 5278 subjects screened at baseline evaluation, 16 were excluded because they

TABLE 2. Baseline demographic and clinical characteristics of cohort stratified by mortality

	Died (n = 2701)	Alive on May 1, 2007 (n = 2561)	*P* value
Age (y)	77.1 ± 7.2 (77.0)	71.3 ± 5.2 (70.0)	< .001
Male sex	1113 (41.2%)	1118 (43.7%)	.073
Geographical area			
Arévalo county (rural area)	995 (36.8%)	929 (36.3%)	.004
Las Margaritas (blue collar area)	859 (31.8%)	915 (35.7%)	
Lista (white collar area)	847 (31.4%)	717 (28.0%)	
Education[a]			
Illiterate	399 (15.0%)	309 (12.1%)	.016
Can read and write	1062 (39.8%)	1026 (40.3%)	
Primary studies	843 (31.6%)	870 (34.1%)	
≥Secondary studies	363 (13.6%)	344 (13.5%)	
Self-reported ever smoker[a]	893 (43.7%)	709 (34.2%)	< .001
Self-reported ever drinker[a]	1160 (56.9%)	1075 (51.9%)	.001
Self-reported hypertension[a]	1397 (55.2%)	1166 (46.9%)	< .001
Self-reported diabetes mellitus[a]	507 (20.2%)	332 (13.4%)	< .001
Self-reported chronic obstructive pulmonary disease[a]	519 (21.1%)	262 (10.7%)	< .001
Self-reported osteoarthritis[a]	1434 (58.5%)	1545 (63.1%)	.001
Self-reported heart disease[a]	353 (13.8%)	154 (6.2%)	< .001
Self-reported depressive symptoms or antidepressant use[a]	600 (26.0%)	580 (25.6%)	.730
Dementia	275 (10.2%)	31 (1.2%)	< .001
Stroke	180 (6.7%)	75 (2.9%)	< .001
Number of medications[a]	2.7 ± 2.0 (2.0)	1.9 ± 1.7 (2.0)	< .001

Mean ± SD (median) is given for age and number of medications. The Mann–Whitney test was used for comparisons of continuous data and the χ^2 test for proportions.
[a]n < 5262 because of missing data.

lacked data on death status. Therefore, the final cohort consisted of 5262 subjects, which included 1142 subjects (21.7%) who had been evaluated using the short form of the questionnaire. At baseline, 3 of 81 PD cases (3.7%) had had PD for 20 or more years, 19 (23.4%) had had PD for 10–19 years, and 59 (72.8%) had had PD for 1–9 years. Age at PD onset ranged from 41 to 84 years (median, 70 years). Baseline Hoehn and Yahr staging was as follows: stage 1, 9 (11.1%); stage 2, 40 (49.4%); stage 3, 12 (14.8%); stage 4, 16 (19.8%); and stage 5, 4 (4.9%). Of the 81 PD cases, 61 (75.3%) were examined by NEDICES neurologists; in the remaining 20, diagnoses were assigned based on medical record review. There were significant differences in age and medical comorbidities when subjects with PD were compared with those without PD (Table 1).

Two thousand seven hundred and one of 5262 subjects (51.3%) died over a median follow-up of 12.0 years (range, 0.04–14.8 years). Subjects who died differed from those who had not (Table 2) with respect to baseline demographic factors and several baseline comorbid conditions. Of the 81 PD cases, 66 (81.5%) died during follow-up, and of the 5181 subjects without PD, 2635 (50.8%) died during the same period (Fig. 1).

In an unadjusted Cox model, risk of mortality was increased in subjects with PD (HR, 2.29; 95% CI, 1.80–2.93; $P < .001$) versus those without PD (reference group). In a Cox model adjusted for age in years, dementia, heart disease, and number of medications (ie, variables that were associated with both PD and death), the risk of mortality remained elevated in subjects with PD (HR, 1.67; 95% CI, 1.30–2.15; $P < .001$; model 1 in Table 3). The results did not change in a Cox model that adjusted for variables associated with either PD or death (age in years, dementia, heart disease, number of medications, education, ever smoker, ever drinker, diabetes mellitus, hypertension,

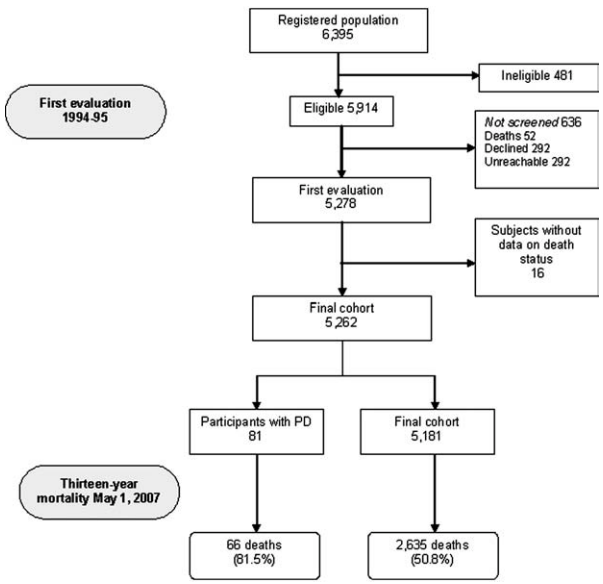

FIG. 1. Flow chart of the study.

TABLE 3. Hazard ratios of mortality in subjects with baseline PD versus those without baseline PD (reference group)

	Unadjusted		Model 1		Model 2	
	Hazard ratio	95% CI	Hazard ratio	95% CI	Hazard ratio	95% CI
Subjects with PD (n = 81)	2.29[a,b]	1.80–2.93	1.67[c]	1.30–2.15	1.75[c]	1.32–2.31
Subjects without PD (n = 5181), reference category	1.00	—	1.00	—	1.00	—

Model 1: adjusted for age in years, dementia, heart disease, and number of medications.
Model 2: adjusted for age in years, dementia, heart disease, number of medications, geographical area, education, ever smoker, ever drinker, diabetes mellitus, hypertension, chronic obstructive pulmonary disease, osteoarthritis, stroke, and depressive symptoms or antidepressant use.
[a]$P < .05$.
[b]$P < .01$.
[c]$P < .001$.

TABLE 4. Hazard ratios of mortality in subjects with baseline PD who had been examined by NEDICES neurologists versus those without baseline PD (reference group)

	Unadjusted		Model 1		Model 2	
	Hazard ratio	95% CI	Hazard ratio	95% CI	Hazard ratio	95% CI
Subjects with PD (n = 61)	2.13[c]	1.60–2.82	1.49[b]	1.18–1.99	1.61[b]	1.19–2.19
Subjects without PD (n = 5181), reference category	1.00	—	1.00	—	1.00	—

Model 1: adjusted for age in years, dementia, heart disease, and number of medications.
Model 2: adjusted for age in years, dementia, heart disease, number of medications, geographical area, education, ever smoker, ever drinker, diabetes mellitus, hypertension, chronic obstructive pulmonary disease, osteoarthritis, stroke, and depressive symptoms or antidepressant use.
[a]$P < .05$.
[b]$P < .01$.
[c]$P < .001$.

chronic obstructive pulmonary disease, osteoarthritis, stroke, and depressive symptoms or antidepressant use; $P < .001$; model 2 in Table 3). In a secondary analysis, we excluded 20 PD patients who had not been examined by NEDICES neurologists. The risk of mortality remained increased in the remaining 61 subjects with PD versus those without PD (reference group); see Table 4.

In additional Cox models, the risk of mortality was higher in PD patients with dementia and in PD patients without dementia when they were compared with the reference group (subjects without PD or dementia; Table 5), although in adjusted models, the HRs were highest in those with PD and dementia. The risk of mortality is also shown in PD patients stratified by Hoehn and Yahr staging (Table 6), by age of disease onset (Table 7), and by disease duration (Table 8).

The Kaplan–Meier curve for overall survival (Fig. 2) showed the PD cohort to be at increased risk of death (log-rank $P < .001$).

PD was only reported as the cause of death in 18.2% of PD cases (Table 9). In both PD cases and subjects without PD, cardiovascular disease was the most frequently reported cause of death. There were no group differences with respect to this or other non-PD causes of death (Table 9).

TABLE 5. Hazard ratios of mortality in subjects with baseline PD stratified by dementia status versus those without baseline PD or baseline dementia (reference group)

	Unadjusted		Model 1		Model 2	
	Hazard ratio	95% CI	Hazard ratio	95% CI	Hazard ratio	95% CI
Subjects with PD and dementia (n = 13)	4.03[c]	2.28–7.10	2.07[a]	1.11–3.86	2.60[b]	1.40–4.90
Subjects with PD but without dementia (n = 68)	4.50[c]	3.95–5.12	2.01[c]	1.53–2.65	2.07[c]	2.19–3.12
Subjects with dementia without PD (n = 293)	2.32[c]	1.77–3.05	2.40[c]	2.08–2.77	2.61[c]	1.53–2.81
Subjects without PD or dementia (n = 4888), reference category	1.00	—	1.00	—	1.00	—

Model 1: adjusted for age in years, heart disease, and number of medications.
Model 2: adjusted for age in years, heart disease, number of medications, geographical area, education, ever smoker, ever drinker, diabetes mellitus, hypertension, chronic obstructive pulmonary disease, osteoarthritis, stroke, and depressive symptoms or antidepressant use.
[a]$P < .05$.
[b]$P < .01$.
[c]$P < .001$.

TABLE 6. Hazard ratios of mortality in subjects with baseline PD stratified by Hoehn & Yahr staging versus those without baseline PD (reference group)

	Unadjusted		Model 1		Model 2	
	Hazard ratio	95% CI	Hazard ratio	95% CI	Hazard ratio	95% CI
PD patients with a Hoehn & Yahr staging of 3, 4, or 5 (n = 32)	2.65[c]	1.81–3.87	2.05[b]	1.38–3.05	2.33[b]	1.49–3.63
PD patients with a Hoehn & Yahr staging of 1 or 2 (n = 49)	2.11[c]	1.54–2.89	1.49[a]	1.07–2.06	1.52[a]	1.07–2.16
Subjects without PD (n = 5181), reference category	1.00	—	1.00	—	1.00	—

Model 1: adjusted for age in years, dementia, heart disease, and number of medications.
Model 2: adjusted for age in years, dementia, heart disease, number of medications, geographical area, education, ever smoker, ever drinker, diabetes mellitus, hypertension, chronic obstructive pulmonary disease, osteoarthritis, stroke, and depressive symptoms or antidepressant use.
[a]$P < .05$.
[b]$P < .01$.
[c]$P < .001$.

TABLE 7. Hazard ratios of mortality in subjects with PD stratified by PD onset versus those without PD (reference group)

	Unadjusted		Model 1		Model 2	
	Hazard ratio	95% CI	Hazard ratio	95% CI	Hazard ratio	95% CI
Elderly-onset (≥65 years) PD patients (n = 19)	2.36	1.79–3.12	1.61[b]	1.21–2.14	1.73[c]	1.28–2.36
Earlier-onset (<65 years) PD patients (n = 62)	2.08[b]	1.25–3.45	1.97[a]	1.14–3.41	1.81	0.96—3.38
Subjects without PD (n = 5181) (reference category)	1.00	—	1.00	—	1.00	—

Model 1: adjusted for age in years, dementia, heart disease, and number of medications.
Model 2: adjusted for age in years, dementia, heart disease, number of medications, geographical area, education, ever smoker, ever drinker, diabetes mellitus, hypertension, chronic obstructive pulmonary disease, osteoarthritis, stroke, and depressive symptoms or antidepressant use.
[a]$P < .05$.
[b]$P < .01$.
[c]$P < .001$.

Discussion

An increased risk of mortality associated with PD has been observed in most prior mortality studies,[1–29] including the 3 studies in which patients were ascertained directly from the population.[12,23,26] Our adjusted estimates of HR, which ranged from 1.67 to 1.75, are slightly lower than those obtained in other community-based studies,[1,4,7,9,12,13,20,23,26] most of which reported a twofold greater risk of mortality. One possible explanation is the low average disease severity (60.5% of the PD subjects had a baseline Hoehn and Yahr stage of 1 or 2; see Results section) in our study, which resulted from our screening methods, through which we identified a large number of previously unrecognized patients with mild PD.[31]

We also found that the adjusted mortality HRs were highest among PD patients with dementia. Only a few studies have investigated to what extent dementia contributes to mortality in PD.[9,18,22,23] Our results are in accordance with these previous observations,[9,18,22,23]

TABLE 8. Hazard ratios of mortality in subjects with PD stratified by PD duration versus those without PD (reference group)

	Unadjusted		Model 1		Model 2	
	Hazard ratio	95% CI	Hazard ratio	95% CI	Hazard ratio	95% CI
PD duration (>5 years) (n = 34)	2.50[c]	1.72–3.63	1.75[b]	1.17–2.62	1.92[b]	1.22–3.03
PD duration (≤5 years) (n = 47)	2.16[c]	1.57–2.98	1.62[b]	1.18–2.24	1.63[b]	1.15–2.29
Subjects without PD (n = 5181), reference category	1.00	—	1.00	—	1.00	—

Model 1: adjusted for age in years, dementia, heart disease, and number of medications.
Model 2: adjusted for age in years, dementia, heart disease, number of medications, geographical area, education, ever smoker, ever drinker, diabetes mellitus, hypertension, chronic obstructive pulmonary disease, osteoarthritis, stroke, and depressive symptoms or antidepressant use.
[a]$P < .05$.
[b]$P < .01$.
[c]$P < .001$.

which indicated that mortality rates are particularly high in PD with dementia. Taken together, the previous results and ours suggest that the reduced life expectancy among patients with PD can be ascribed in part to dementia[9,18,22,23]

The literature provides limited data on cause of death in PD, and much of the data are based on death certificates. In the NEDICES study, cardiovascular diseases were the most frequent cause of death in persons with PD, and in this respect, PD cases were similar to people in the general population.

Our study had limitations. First, we only included individuals aged 65 and older; the NEDICES study, in which this study was nested, was a study of the elderly (age 65 years and older). However, the prevalence and incidence of PD increase with age, with the disease burden being of most importance in older age groups.[31,32] Second, we assessed depressive symptoms by self-report, and although our screening question was modeled on a question that correctly diagnosed depression in 85.4% of subjects,[43] we may have underascertained depression. However, based on a validation study in which we showed a high level of agreement between the data generated from this screening question and a more detailed in-person psychiatric assessment,[43] we think that such misclassification errors were likely to be low. Third, in the Cox proportional hazards analyses, we estimated the risks of mortality as a function of baseline factors (PD, dementia, etc.) and did not take into consideration a change in these factors after the baseline visit (eg, new onset [incident] PD at follow-up). In this study, only prevalent PD cases were included. Table 8 indicates that those with PD duration greater than 5 years had a higher HR for mortality than those with PD duration less than or equal to 5 years. Hence, by not including incident PD cases, our overall estimate of the HR for mortality may be high.

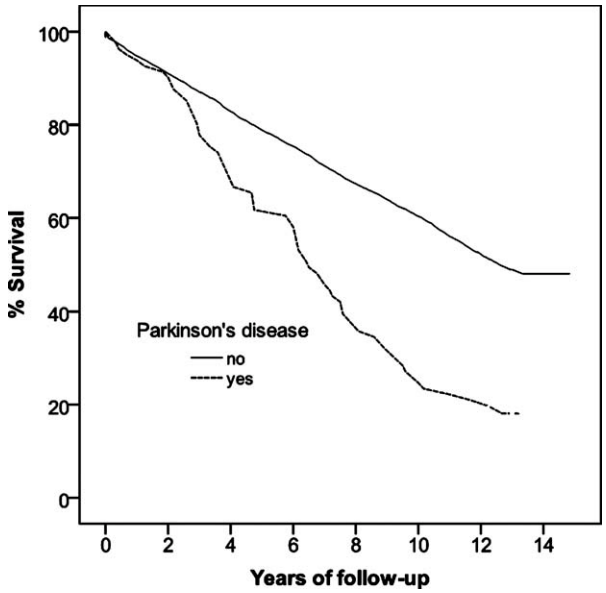

FIG. 2. Kaplan–Meier curves of percent survival for subjects with and without PD (log-rank $P < .001$). Of the 81 PD cases, 66 (81.5%) died during follow-up, and of the 5181 subjects without PD, 2635 (50.8%) died during the same period. In a Cox model that adjusted for age in years, dementia, heart disease, and number of medications, the risk of mortality was elevated in subjects with PD (HR, 1.67; 95% CI, 1.30–2.15; $P < .001$).

TABLE 9. Primary cause of death (IDC 9th) by diagnostic groups

	Subjects with Parkinson's disease, n (%)	Subjects without Parkinson's disease, n (%)	*P* value
Parkinson's disease	12 (18.2%)	3 (0.1%)	.0001
Dementia	3 (4.5%)	178 (6.8%)	Not significant
Cerebrovascular disorders	5 (7.6%)	224 (8.5%)	Not significant
Cardiovascular diseases	14 (21.2%)	743 (28.2%)	Not significant
Respiratory diseases	9 (13.6%)	378 (14.3%)	Not significant
Cancer	9 (13.6%)	650 (24.7%)	Not significant
Other	14 (21.2%)	459 (17.4%)	Not significant
Total	66 (100%)	2635 (100%)	

χ^2 test or Fisher's exact test was used for comparison of proportions.

This study also has several strengths. First, case ascertainment for PD was ensured in most cases through in-person instead of record-based screening methods. Second, we attempted to adjust for the effects of numerous potential confounders. Third, the controls were selected from the same population as the cases. Fourth, the study was population based, allowing us to assess a group of patients with relatively mild PD unselected for medical treatment or surgery. Finally, we had complete death information of almost the entire cohort (99.7%).

Data from the NEDICES study have provided new estimates of risk of PD-related mortality in a large population-based cohort. The data presented here provide further information for the projection of PD mortality rates in Western countries. ■

Acknowledgments: We gratefully acknowledge the vital help of the other members of the NEDICES Study Group: S. Vega, J.M. Morales, R. Gabriel, A. Portera-Sánchez, A. Berbel, A. Martínez-Salio, J. Díaz-Guzmán, J. Olazarán, J. Pardo, J. Porta-Etessam, F. Pérez del Molino, J. Rivera-Navarro, M. Alonso, C. Gómez, C. Saiz, G. Fernández, P. Rodríguez, and F. Sánchez-Sánchez. Finally, we also express our sincere thanks to J. de Pedro-Cuesta and J. Almazán, the municipal authorities, family doctors, nurses, and the populations of Getafe, Lista, and Arévalo counties.

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