

PREVALENCE OF PARKINSONIAN SIGNS AND ASSOCIATED MORTALITY IN A COMMUNITY POPULATION OF OLDER PEOPLE

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Abstract Background. Older people frequently have signs of parkinsonism, but information about the prevalence of parkinsonism and mortality among those with the condition in the community is limited.

Methods. A stratified random sample of 467 residents of East Boston, Massachusetts, 65 years of age or older, were given structured neurologic examinations. Using uniform, specified combinations of parkinsonian signs, we estimated the prevalence of four categories of signs — bradykinesia, gait disturbance, rigidity, and tremor — and of parkinsonism, defined as the presence of two or more categories. We did not study Parkinson's disease because it could not be distinguished from other conditions that can cause parkinsonism. Proportional-hazards models were used to compare the risk of death among people with and those without parkinsonism.

Results. One hundred fifty-nine persons had parkinsonism, 301 did not, and 7 could not be classified. The

overall prevalence estimates were 14.9 percent for people 65 to 74 years of age, 29.5 percent for those 75 to 84, and 52.4 percent for those 85 and older. With a mean follow-up period of 9.2 years, 124 persons with parkinsonism (78 percent) and 146 persons without it (49 percent) died. Adjusted for age and sex, the overall risk of death among people with parkinsonism was 2.0 (95 percent confidence interval, 1.6 to 2.6) times that among people without it. Among people with parkinsonism, the presence of gait disturbance was associated with an increased risk of death.

Conclusions. Parkinsonism is very common among people over the age of 65, and its prevalence increases markedly with age. Parkinsonism is associated with a twofold increase in the risk of death, which is strongly related to the presence of a gait disturbance. (N Engl J Med 1996;334:71-6.)

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SIGNS of parkinsonism¹⁻³ are frequently found on neurologic examination of older people.⁴⁻⁹ Although these signs are often considered to be benign concomitants of aging,^{10,11} data regarding their prevalence and relation to mortality are derived primarily from studies conducted in people who have come to medical attention.¹²⁻¹⁷ Because the proportion of all the people with parkinsonism who come to medical attention is unknown and may be small, such studies are unlikely to capture the full spectrum of parkinsonism in the general population. There have been few population-based studies of parkinsonism.¹⁸

We estimated the prevalence of parkinsonian signs assessed by a structured neurologic examination as part of a community study of common health problems of older people. Using uniform, specified combinations of parkinsonian signs, we estimated the prevalence of four categories of signs — designated as bradykinesia, gait disturbance, rigidity, and tremor — and of parkinsonism, which was defined as the presence of two or more categories. Over a nine-year period, we examined the relation between parkinsonism at the base-line clinical evaluation and subsequent mortality. We could not determine the prevalence of Parkinson's disease or mortality associated with it because our study design did not allow us to distinguish this condition from others that cause parkinsonism, such as Alzheimer's disease, subcortical vascular disease, and multisystem atrophy.

METHODS

Subjects

Participants were residents of East Boston, Massachusetts, an urban community of 32,000 people, and were 65 years of age or older when

the study began. The community is primarily composed of low- and middle-income working-class people, many of Italian-American descent. East Boston is one of the four centers of the National Institute on Aging's Established Populations for Epidemiologic Studies of the Elderly project.¹⁹ The study was approved by the Committee for the Protection of Subjects from Research Risks at Brigham and Women's Hospital, Boston, and all participants provided written informed consent.

Study Design

A complete door-to-door census of the community was carried out in 1982-1984. All residents 65 years of age or older were asked to participate in a structured interview that assessed common medical and social problems of older people. Of the 4485 community residents 65 or older, 3622 (80.8 percent) participated. The interview included brief tests of immediate and delayed memory.^{20,21} A random sample of 714 persons, stratified according to age, sex, and memory performance, with older groups sampled more heavily, was identified for a detailed clinical evaluation; 54 of them died before being invited to be evaluated. Beginning in 1984 (an average of 16 months after the initial interview), 467 of the 660 surviving eligible people (70.8 percent) underwent structured neurologic examinations, neuropsychological performance testing, and laboratory testing; in addition, for each participant, all medications were identified, a medical history was taken, and an interview was conducted with an informant who knew the participant well. This sample has been used previously to estimate the prevalence of Alzheimer's disease and neurologic-examination findings in the community and the relation of Alzheimer's disease to mortality; more details of the study design and sampling procedures have been reported previously.²²⁻²⁴

Clinical Evaluation

Most evaluations were performed by one board-certified neurologist. The medical history included the identification of all medications used to treat Parkinson's disease. A complete neurologic examination was performed, including a uniform, structured assessment of parkinsonian signs. Cranial nerves, extremity strength, deep-tendon reflexes, extensor plantar responses, abnormal movements, frontal-releasing signs, praxis, and position sensation and vibratory sensation in the feet were also tested. A diagnosis of Parkinson's disease was based on the clinician's judgment and required paucity of movements of both face and extremities, an abnormal gait with a reduced arm swing, slowed finger taps, and the absence of weakness and other corticospinal tract signs; other parkinsonian signs were supportive but not obligatory. A diagnosis of Alzheimer's disease satisfied the criteria of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Dis-

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orders Association.²⁵ The content of the clinical evaluations and the diagnostic classifications of participants have been described previously.^{23,26}

Assessment of Parkinsonian Signs, Sign Categories, and Parkinsonism

A uniform, structured neurologic examination was used to determine the presence of 12 individual parkinsonian signs. Parkinsonian signs were sorted into four categories of motor signs of parkinsonism: bradykinesia (paucity of movements of the extremities and face and slow finger taps), gait disturbance (shuffling gait, reduced arm swing, and prolonged turning), rigidity (in each extremity), and tremor (resting and postural). Postural-reflex impairment was not explicitly tested. To minimize the effect of an isolated poor performance on the clinical classification of parkinsonism, two or more signs within the category were required to be present for a patient to be considered to have a parkinsonian-sign category (with the exception of the tremor category, for which there was only one sign of resting tremor and one of postural tremor). Parkinsonism was defined as the presence of two or more parkinsonian-sign categories¹⁻³ (Table 1).

Statistical Analysis

We calculated estimates of age-specific prevalences for parkinsonian signs, sign categories, and parkinsonism using a two-step procedure, as previously described.²² Prevalences were estimated for each sex and age group from a logistic-regression model based on the clinical-evaluation sample. These estimates were then weighted to adjust for unequal sampling from the East Boston population and combined to give estimates for 10-year age groups. Tests for a trend in prevalence with increasing age were based on the coefficient for age in the logistic-regression model used to obtain smoothed prevalence estimates in the first step.

The primary end point was death from any cause. Complete follow-up data on vital status were available through December 31, 1992. Information about deaths was obtained by systematic review of the National Death Index and from interviews with knowledgeable informants. For secondary analyses, a trained researcher, blinded to data on parkinsonism, reviewed death certificates to determine the underlying and immediate causes of death. These were coded according to the *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM).²⁷ The analysis included participants whose deaths were due to any respiratory disease (ICD-9-CM codes 460 to 519), chronic obstructive airway disease (codes 490 to 496), pneumonia (codes 480 to 487, and 507), any cardiovascular disease (codes 390 to 459), any cerebrovascular disease (codes 430 to 438), any cancer (codes 140 to 239), or injury (ICD-9-CM "E" codes).

Proportional-hazards models were used to compare the relative risk of death among people with parkinsonism with that among unaffected people, with adjustments for age and sex.²⁸ These models treated the log of the instantaneous rate of mortality at each time point in the study, among those who had survived at least that long since the clinical evaluation, as increasing linearly with age for both men and

Table 1. The Specified Combinations of 12 Parkinsonian Signs Used to Define Four Parkinsonian-Sign Categories and Parkinsonism.

PARKINSONIAN SIGN	SIGN CATEGORY	PARKINSONISM
Paucity of movements of the extremities	Bradykinesia = at least two of the three bradykinesia signs	Parkinsonism = at least two of the four parkinsonian-sign categories
Paucity of movements of the face		
Slow finger taps		
Reduced arm swing	Gait disturbance = at least two of the three gait-disturbance signs	
Shuffling gait		
Prolonged turning		
Right-arm rigidity	Rigidity = at least two of the four rigidity signs	
Left-arm rigidity		
Right-leg rigidity		
Left-leg rigidity		
Resting tremor	Tremor = at least one sign of tremor	
Postural tremor		

Table 2. Age-Specific Estimates of the Prevalence of Parkinsonian Signs.*

PARKINSONIAN SIGN	NO. IN SAMPLE	PREVALENCE ACCORDING TO AGE			P VALUE FOR TREND (AGE)
		65-74 YR	75-84 YR	≥85 YR	
<i>percent</i>					
Bradykinesia					
Paucity of movements of the extremities	98	9.3±2.0	16.6±2.0	30.1±3.8	<0.001
Paucity of movements of the face	116	12.6±2.4	21.2±2.2	35.5±4.0	<0.001
Slow finger taps	197	22.8±3.3	40.0±2.7	62.5±3.9	<0.001
Gait disturbance					
Reduced arm swing	210	24.4±3.3	41.8±2.7	64.8±3.9	<0.001
Shuffling gait	83	6.4±1.6	13.8±1.8	29.7±3.8	<0.001
Prolonged turning	153	15.7±2.7	29.6±2.5	50.8±4.1	<0.001
Rigidity					
Right leg	141	16.7±2.8	27.6±2.4	43.3±4.1	<0.001
Left leg	154	16.9±2.8	28.6±2.4	46.3±4.1	<0.001
Right arm	62	8.7±2.1	12.0±1.7	17.2±3.1	0.046
Left arm	69	9.8±2.3	14.4±1.9	20.7±3.4	0.009
Tremor					
Postural	99	16.5±2.9	20.7±2.2	25.6±3.5	0.02
Resting	24	6.1±2.0	5.6±1.3	5.0±1.8	0.681

*Plus-minus values are prevalence estimates ±SE.

women, but allowed men to have different mortality rates overall. The model was validated to ensure that the effect of parkinsonism on mortality was not a result of inadequate accounting for the relation of mortality to age or of a clinical diagnosis of Alzheimer's disease.²⁴ To be sure that any association of parkinsonism with mortality was not partly an artifact of the sample design that would not be evident in the whole population, separate logistic regressions, adjusted by pseudo-maximum-likelihood estimation for the sampling design, were carried out, with survival at successive years of follow-up used as the outcome.²⁹ This analysis was consistent with proportional-hazards models and showed similar risks of death throughout the entire study period. Similar models were used for secondary analyses. Kaplan-Meier curves were used to display the results.²⁸

RESULTS

Prevalence of Parkinsonian Signs and Sign Categories

Parkinsonian signs were common. The proportion of people with each sign in each of the age groups is shown in Table 2. Percentages were weighted to reflect the sampling design. The prevalence of each parkinsonian sign except resting tremor increased significantly with age.

Factor analysis was used to assess the degree to which the associations among the 12 parkinsonian signs corresponded to the specified groupings.³⁰ Four factors were identified that, in general, supported the placing of motor signs in the four categories of bradykinesia, gait disturbance, rigidity, and tremor (data not shown). Therefore, the four sign categories were used in subsequent analyses. The number of people in whom each category was present and the prevalence (weighted to reflect the sampling design) of each sign category are given in Table 3. All sign categories were common, and their prevalence was strongly related to age. The prevalence of gait disturbance was higher in women; rigidity and tremor were more common in men.

Prevalence of Parkinsonism

Of the 467 persons who were clinically evaluated, 159 had parkinsonism and 301 did not (7 could not be clas-

Table 3. Age-Specific Estimates of the Prevalence of Parkinsonian-Sign Categories and Parkinsonism.*

SIGN AND AGE GROUP (YR)	NO. IN SAMPLE	ALL PARTICIPANTS	P VALUE FOR TREND (AGE)	PREVALENCE		P VALUE FOR TREND (SEX)
				MEN	WOMEN	
				percent		
Bradykinesia	114		<0.001			0.762
65–74		11.1±2.2		10.7±2.4	11.4±2.5	
75–84		20.6±2.2		19.7±2.9	21.0±2.7	
≥85		37.1±4.1		36.5±5.3	37.5±4.4	
Gait disturbance	152		<0.001			0.017
65–74		13.0±2.4		9.6±2.1	15.3±2.9	
75–84		27.6±2.4		21.2±2.9	31.2±3.2	
≥85		51.6±4.1		44.6±5.3	55.6±4.4	
Rigidity	149		<0.001			0.031
65–74		19.2±3.0		23.5±3.8	16.4±3.2	
75–84		29.5±2.5		35.2±3.6	26.3±3.0	
≥85		43.5±4.1		50.3±5.3	39.5±4.4	
Tremor	113		0.018			0.031
65–74		19.1±3.1		23.6±4.0	16.2±3.2	
75–84		24.2±2.3		29.8±3.4	21.0±2.8	
≥85		30.1±3.7		36.8±5.2	26.2±3.9	
Parkinsonism	159		<0.001			0.969
65–74		14.9±2.6		14.7±2.8	15.0±2.9	
75–84		29.5±2.5		29.1±3.4	29.7±3.2	
≥85		52.4±4.2		53.0±5.4	52.1±4.5	

*Plus-minus values are prevalence estimates ±SE.

sified). The prevalence of parkinsonism, weighted to reflect the sampling design, is shown in Table 3. Parkinsonism was very common, and its prevalence increased strongly with age but was unrelated to sex. The overall prevalence estimate for people 65 to 74 years of age was 14.9 percent; this increased to 29.5 percent for those 75 to 84 and to 52.4 percent for those 85 and older.

Fifteen of the 159 persons with parkinsonism had a clinical diagnosis of Parkinson’s disease. Seven of these were taking levodopa.

Parkinsonism and Risk of Death

The average length of follow-up was 9.2 years. There were 276 deaths — 124 of 159 persons with parkinsonism (78 percent), 146 of 301 persons without parkinsonism (49 percent), and 6 of 7 persons not classified. The crude association between a diagnosis of parkinsonism and death at any time during the follow-up period is shown, according to five-year age groups, in Table 4. In all age groups, the proportion of deaths was higher among those with parkinsonism.

We examined the risk of death associated with parkinsonism, adjusting simultaneously for the confounding effects of age and sex. A proportional-hazards model was constructed that compared the risk of death among people with parkinsonism with that among people without it. The overall risk of death among those with parkinsonism was 2.0 times that among those without it (95 percent confidence interval, 1.6 to 2.6). Kaplan–Meier survival curves through eight years of follow-up are shown in Figure 1. When an indicator for Alzheimer’s disease at the base-line evaluation was included in the same model, the results were virtually identical.

To ensure that the complex stratified sampling did not

distort the relation between parkinsonism and mortality and that the results based on the follow-up of the sample represented the population, we carried out separate logistic-regression analyses at successive years of follow-up, using survival as the outcome. These analyses were consistent with the results of the proportional-hazards model (data not shown). Secondary analyses based on the underlying and immediate causes of death as coded according to the ICD-9-CM suggested that the excess mortality among those with parkinsonism was not due to any single group of diagnoses (data not shown).

Parkinsonian-Sign Categories and Risk of Death

Parkinsonism is a heterogeneous condition reflecting the occurrence of various combinations of motor-sign categories. To examine the association between the number of parkinsonian-sign categories and mortality, a model was constructed that included separate terms for two, three, and four sign categories. The risk ratio for death for two categories was 1.9 (95 percent confidence interval, 1.4 to 2.5); it was 2.0 for three categories (95 percent confidence interval, 1.3 to 3.0) and 2.6 (95 percent confidence interval, 1.4 to 4.8) for all four categories.

To assess the relation between individual sign categories and mortality, a proportional-hazards model was constructed that included separate terms for each category. This model suggested that after adjustment for the other sign categories, only gait disturbance was associated with an increased risk of death. The risk ratio for bradykinesia was 1.3 (95 percent confidence interval, 0.9 to 1.7); for gait disturbance, 2.3 (95 percent confidence interval, 1.7 to 3.1); for rigidity, 1.0 (95 percent confidence interval, 0.7 to 1.3); and for tremor, 1.0 (95 percent confidence interval, 0.8 to 1.3).

We then constructed a proportional-hazards model comparing the risk of death among people with parkin-

Table 4. Crude Association between Parkinsonism and Death at Any Time during the Follow-up Period, According to Age Group.

AGE GROUP (YR)	PARKINSONISM*		ALL PARTICIPANTS
	PRESENT	ABSENT	
	no. of deaths/no. in group (%)		
65–69	5/7 (71)	15/42 (36)	20/49 (41)
70–74	10/20 (50)	19/66 (29)	29/86 (34)
75–79	20/25 (80)	23/62 (37)	43/87 (49)
80–84	34/44 (77)	35/58 (60)	69/102 (68)
≥85	55/63 (87)	54/73 (74)	109/136 (80)
Total	124/159 (78)	146/301 (49)	270/460 (59)

*Seven persons could not be classified according to whether parkinsonism was present or absent.

sonism who had gait disturbance, and the risk among those with parkinsonism without gait disturbance, with the risk among those without parkinsonism. As compared with those without parkinsonism, people with parkinsonism and gait disturbance had a relative risk of death of 2.4 (95 percent confidence interval, 1.8 to 3.1; $P < 0.001$); among those with parkinsonism without gait disturbance the relative risk was 1.1 (95 percent confidence interval, 0.7 to 1.8; $P = 0.716$). Kaplan–Meier survival curves through eight years of follow-up are shown in Figure 2.

In older persons, gait disturbance may be associated with many conditions in addition to parkinsonism.^{31,32} Logistic regression was used to determine the extent to which gait disturbance was associated with each of the other sign categories. Among people with gait disturbance, the odds ratios were as follows: for bradykinesia, 12.0 (95 percent confidence interval, 7.0 to 20.5; $P < 0.001$); for rigidity, 1.8 (95 percent confidence interval, 1.2 to 2.8; $P < 0.05$); and for tremor, 2.2 (95 percent confidence interval, 1.4 to 3.6; $P < 0.001$).

DISCUSSION

These data suggest that parkinsonism is very common among people over the age of 65 and that its prevalence increases strongly with age. Parkinsonism is associated with a twofold increase in the risk of death, which is strongly related to the presence of a gait disturbance.

A previous population-based study, conducted in three municipalities in Sicily, examined age-specific prevalences of parkinsonism.¹⁸ The authors reported a similar association with age, but lower estimates for the prevalence of parkinsonism. They did not examine the prevalence of individual parkinsonian signs or sign categories. Indirect evidence of the frequency of parkinsonian signs comes from population-based studies in the Washington Heights and Inwood areas of New York City.

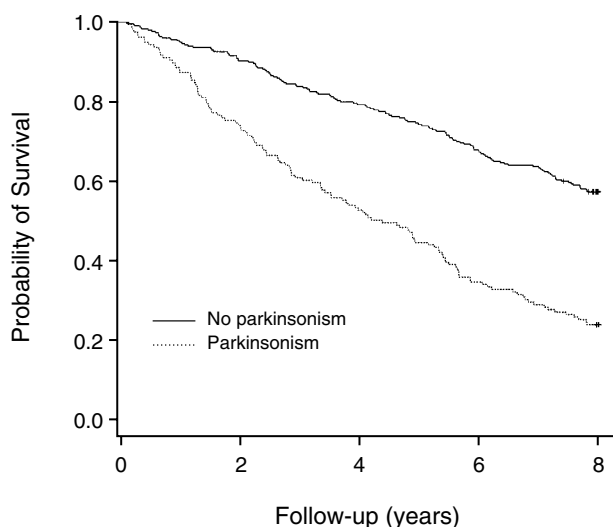


Figure 1. Kaplan–Meier Survival Curves for 159 Persons with Parkinsonism and 301 Persons without Parkinsonism through Eight Years of Follow-up.

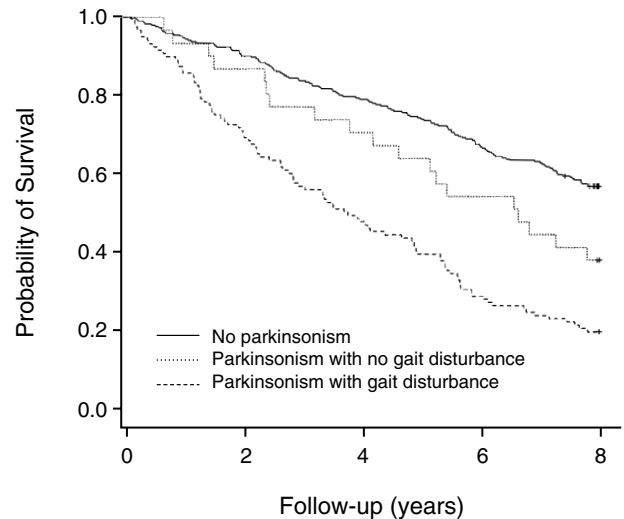


Figure 2. Kaplan–Meier Survival Curves for 159 Persons with Parkinsonism — 128 Who Had Gait Disturbance and 31 Who Did Not — and for 301 Persons without Parkinsonism through Eight Years of Follow-up.

These studies showed a slightly lower frequency of parkinsonian signs among people without overt neurologic disease who underwent detailed clinical evaluations.⁴ Differences in definitions of parkinsonism between studies may have contributed to our higher prevalence estimates. The transition to mild parkinsonism is gradual.³³ In community settings, where mild parkinsonism is likely to predominate, even small differences in the distinction between the presence or absence of parkinsonism could substantially affect estimates of prevalence.

Several studies have evaluated the risk of death associated with parkinsonism among people who came to medical attention. Hoehn and Yahr¹³ reported that, among people evaluated at a specialty clinic, the risk of death associated with parkinsonism was approximately three times that reported for the general population of the same age, race, and sex and that the risk of death was greater among those with manifestations of parkinsonism other than tremor. Three studies that identified people with parkinsonism or Parkinson's disease from medical registries reported that the risk of death was between 1.6 and 2.6 times that of controls.^{12,16,17} Among people with Parkinson's disease, impaired gait and posture, assessed with the Webster scale,³⁴ were associated with increased mortality.¹⁷

Previous studies of people with Parkinson's disease who came to medical attention suggest that such people are at greater risk of death from respiratory diseases,¹⁷ ischemic heart disease,¹⁶ and cerebrovascular disease¹⁶ but are at a lower risk of death from cancer.¹³ Our data did not show any differences in the immediate or underlying causes of death on death certificates between people with parkinsonism and those without it.

Two methodologic features of our study increase the reliability of the results. All the people from a geographically defined community could be considered for participation, and the actual rates of participation and fol-

low-up were high. We evaluated parkinsonian signs as part of a structured general neurologic examination and used specified combinations of parkinsonian signs to document the presence of each sign category and to define parkinsonism. Although it has infrequently been applied to parkinsonism, this approach has been used successfully with other chronic neurologic conditions (e.g., cognitive impairment) and is generally considered to be more precise than global clinical impressions.³⁵⁻³⁷ In other studies, criteria for determining the presence or absence of parkinsonian-sign categories and parkinsonism were often not specified. Studies that rely on reviewing of medical records to determine the presence or absence of parkinsonism may underestimate prevalence and overestimate mortality because people with mild parkinsonism may not seek medical attention or their physicians may not diagnose their parkinsonism.

Our study had several limitations. Parkinsonism may result from several disorders that share common clinical features.^{31,38} Our study design did not allow us to differentiate Parkinson's disease from other conditions that cause parkinsonism. Some of the parkinsonism we found probably represents mild, subclinical Parkinson's disease.³² Our finding that resting tremor had the lowest estimated prevalence of the 12 parkinsonian signs is noteworthy; some investigators have suggested that the presence of resting tremor is the most specific sign of Parkinson's disease.^{39,40}

The motor examination did not correspond directly to scales specifically used to quantify motor function in Parkinson's disease.^{41,42} Some relevant parkinsonian signs were not explicitly assessed. Postural-reflex impairment, rather than gait disturbance, is now used in studies of parkinsonism because gait disturbance may be associated with many conditions other than parkinsonism, especially among older people.^{43,44} Several lines of reasoning support the gait-disturbance sign category as part of a parkinsonian syndrome: the items in the neurologic examination were chosen to reflect parkinsonism, factor analysis suggested that gait disturbance was strongly related to bradykinesia (data not shown), and logistic regression demonstrated that gait disturbance was strongly associated with each of the other sign categories.

We examined the relation to subsequent mortality of parkinsonism only at the base-line evaluation. Since the prevalence of parkinsonism in older people appears to double with each additional decade of life, parkinsonism is likely to develop before death in many people classified as not having the condition at base line. Other than the number of signs present, there was no measure of the severity of parkinsonism. The relative proportions of mild, moderate, and severe parkinsonism could not be determined. It is likely that much of the parkinsonism was mild; this would be consistent with population-based data for other chronic neurologic conditions.²³ It is possible that the estimates of the prevalence of parkinsonism would have been higher if people living in institutions had been included.

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