Prevalence of parkinsonism and Parkinson's disease in Europe: the EUROPARKINSON collaborative study

M C de Rijk, C Tzourio, M M B Breteler, J F Dartigues, L Amaducci, S Lopez-Pousa, J M Manubens-Bertran, A Alpérovitch, W A Rocca, for the EUROPARKINSON Study Group*

Department of Epidemiology and Biostatistics, Erasmus University Medical School, Rotterdam, The Netherlands
M C de Rijk
M M B Breteler

Department of Neurology, University Hospital Rotterdam, The Netherlands
M C de Rijk

INSERM Unité 360, Hôpital de La Salpêtrière, Paris, France
C Tzourio
A Alpérovitch

Department of Neurology, Pellegrin Hospital, University of Bordeaux II, France
J F Dartigues

INSERM Unité 360, University of Bordeaux II, France
J F Dartigues

Department of Neurology, University of Florence, Florence, Italy
L Amaducci

Department of Neurology, Santa Caterina Hospital, Girona, Spain
S Lopez-Pousa

Department of Neurology, University of Navarra, Pamplona, Spain
J M Manubens-Bertran

Department of Health Sciences Research, Mayo Clinic and Mayo Foundation, Rochester, Minnesota, USA
W A Rocca

Correspondence to:
Dr A Alpérovitch, INSERM Unité 360, Hôpital La Salpêtrière, 75651 Paris Cedex 13, France.

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*All collaborators are listed at the end of the manuscript

Abstract

***Objectives*—To assess and compare the prevalence of parkinsonism and Parkinson's disease in five European populations that were surveyed with similar methodology and diagnostic criteria.**

***Methods*—Joint analysis of five community surveys—Gironde (France), eight centres in Italy, Rotterdam (The Netherlands), Girona (Spain), and Pamplona (Spain)—in which subjects were screened in person for parkinsonism. Overall, these surveys comprised 14 636 participants aged 65 years or older.**

***Results*—The overall prevalence (per 100 population), age adjusted to the 1991 European standard population, was 2·3 for parkinsonism and 1·6 for Parkinson's disease. The overall prevalence of parkinsonism for the age groups 65 to 69, 70 to 74, 75 to 79, 80 to 84, and 85 to 89 years was respectively, 0·9, 1·5, 3·7, 5·0, and 5·1. The corresponding age specific figures for Parkinson's disease were 0·6, 1·0, 2·7, 3·6, and 3·5. After adjusting for age and sex, the prevalence figures did not differ significantly across studies, except for the French study in which prevalence was lower. Prevalence was similar in men and women. Overall, 24% of the subjects with Parkinson's disease were newly detected through the surveys.**

***Conclusions*—Prevalence of both parkinsonism and Parkinson's disease increased with age, without significant differences between men and women. There was no convincing evidence for differences in prevalence across European countries. A substantial proportion of patients with Parkinson's disease went undetected in the general population.**

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Keywords: Parkinson's disease; parkinsonism; prevalence

Parkinson's disease is one of the most common chronic neurodegenerative diseases in elderly people. Prevalence estimates of Parkinson's disease vary widely across studies and countries[1] but the interpretation of this geographic variation is hampered by differences in methodology and diagnostic criteria. Consequently, it remains unclear whether a true variation exists. As part of the European Community Concerted Action on the Epidemiology of Parkinson's disease (EUROPARKINSON),[2] we conducted a collaborative comparison of five European prevalence surveys of all types of parkinsonism, including Parkinson's disease.

Methods

EUROPARKINSON is a collaborative effort to study the prevalence, incidence, and determinants of Parkinson's disease in Europe comprising five studies, one each from France,[3] Italy,[4] and the Netherlands,[5] and two from Spain. All five studies are community surveys of both independently living and institutionalised elderly subjects 55 years of age or older, with a sample size of at least 1000. Table 1 summarises the characteristics of the five study populations.

CASE FINDING PROCEDURES

All studies used a two phase design to assess the prevalence of parkinsonism and Parkinson's disease. In phase 1, participants were screened in person using a symptom

Table 1 Characteristics of the study populations

Population	*Investigators*	*Geographic location*	*Urban or rural*	*Size of study population*	*Response rate (%)*	*Age (y)*	*Type of sample*	*Years of survey*
France Gironde	Dartigues *et al*	Gironde region	Urban and rural	3149	71	65+	Stratified random sample	1988–9
Italy Eight centres	Amaducci *et al*	Eight provinces across Italy	Urban and rural	4510	80	65+	Stratified random sample	1992–4
The Netherlands Rotterdam	Breteler *et al*	City of Rotterdam, Ommoord district	Urban	6969†	68	55+	Complete enumeration	1990–3
Spain Girona	Lopez-Pousa *et al*	Group of villages in Girona province	Rural	1450	84	70+	Complete enumeration	1990–1
Spain Pamplona	Manubens-Bertran *et al*	City of Pamplona	Urban	1127	82	70+	Stratified random sample	1991

†In the present comparison, persons aged 55 to 64 years (n = 2569) who participated in the Rotterdam study were excluded.

Table 2 Case finding procedures

	Phase 1		*Phase 2*	
Population	*Screening procedure**	*Personnel*	*Diagnostic protocol*	*Personnel*
France Gironde*	*Questions:* Tremor plus rigidity or bradykinesia, antiparkinsonian drugs	Psychologists	Structured clinical work up (UPDRS,† neurological examination)	Neurologists
Italy Eight centres*	*Questions:* Tremor, previous diagnosis, antiparkinsonian drugs *Neurological examination:* Walking on heels, elbow tone	Trained interviewers Physicians	Structured clinical work up (UPDRS,† neurological examination)	Neurologists
The Netherlands, Rotterdam	*Questions:* Previous diagnosis, antiparkinsonian drugs *Neurological examination:* Resting tremor, rigidity or cogwheeling, bradykinesia, impaired postural reflexes	Trained interviewers Physicians	Structured clinical work up (UPDRS,† neurological examination)	Neurologists
Spain Girona	*Questions:* Tremor, previous diagnosis, antiparkinsonian drugs *Neurological examination:* Tremor, rigidity, bradykinesia	Physicians Physicians	Structured clinical work up (UPDRS,† neurological examination)	Neurologists
Spain Pamplona‡	*Questions:* Previous diagnosis, antiparkinsonian drugs *Neurological examination:* Tremor, gait disturbances, clinical impression	Physicians Physicians	Structured clinical work up (UPDRS,† neurological examination)	Neurologists

*Screening was positive if at least one of the screening items was positive. In the institutionalised subjects from the French study, the phase 2 procedures were directly applied without any screening.
†UPDRS = Unified Parkinson's disease rating scale.[23]
‡Screening was positive if at least one question was answered positively or two signs were present at the screening examination.

questionnaire and a brief physical examination. Those who screened positive were extensively evaluated by neurologists in phase 2. The only exception was the study in France in which the physical examination was not used to screen independently living subjects, and all institutionalised participants were examined by a neurologist without any screening. Table 2 presents details of the screening procedures used in each study.

DIAGNOSTIC CRITERIA

With two exceptions, the five studies adhered to common diagnostic criteria for parkinsonism and Parkinson's disease. Parkinsonism was diagnosed when at least two of four cardinal signs (resting tremor, rigidity, bradykinesia, and impaired postural reflexes) were present in a subject not receiving antiparkinsonian medication, or if one or more cardinal signs, documented by medical history, were improved by antiparkinsonian treatment. However, in the study from France, untreated patients with an isolated typical resting tremor were also included. In the study from Girona, Spain, only untreated patients with at least three cardinal signs or treated patients with at least two cardinal signs were included. Parkinson's disease was defined among those affected by parkinsonism by exclusion of all other possible causes. Parkinsonism associated with other causes included: (1) parkinsonism in dementia (onset of dementia clearly before the occurrence of parkinsonism); (2) parkinsonism with associated features (for example, multiple system atrophy or progressive supranuclear palsy); (3) drug induced parkinsonism (parkinsonism after the use of neuroleptic or other antidopaminergic drugs in the six months preceding onset of symptoms and with no history of parkinsonism); (4) vascular parkinsonism (clear time relation between a cerebrovascular event and onset of atypical parkinsonism, preferably supported by neuroimaging, usually without tremor); and (5) unspecified parkinsonism. Included in this last category were patients with no clear time relation between the possible cause (for example, dementia, antidopaminergic drugs) and parkinsonism, or with more than one possible cause. Patients otherwise fulfilling the criteria for Parkinson's disease who showed no progression of the disease over 15 years or were not responsive to antiparkinsonian drugs were considered "unspecified". To increase reliability across studies, the medical records of most parkinsonian subjects were reviewed by an adjudication panel composed of neurologists from each of the participating centres.

DATA ANALYSIS

We calculated age and sex specific prevalence figures of parkinsonism and Parkinson's disease for each survey separately, and for all studies combined. The overall prevalence was directly age standardised with the 1991 European population. The prevalence estimates are presented by five year age groups. To obtain stable prevalence estimates, age groups with less than 10 subjects in the denominator were discarded. As the study from France oversampled institutionalised subjects, prevalence estimates in this study were weighted for the sampling fraction. The prevalence estimates for the age range from 65 to 90 years (70 to 90 years for the two studies from Spain) were also displayed in graphical form, plotted in the middle of the corresponding age group. For the three smallest studies (the French and the two Spanish studies), we presented the data graphically by 10 year age groups to obtain a curve not influenced by

Table 3 Age and sex specific prevalence (per 100 population) of parkinsonism and overall age and sex adjusted prevalence ratios*

Population		Age group (y)†							Prevalence ratio (95% CI)
		65–69	70–74	75–79	80–84	85–89	90–94	95–99	
France Gironde‡	Women	0·6 (4/667)	1·2 (8/656)	2·8 (14/507)	3·2 (16/496)	3·8 (13/340)	5·3 (6/113)	28·6 (8/28)	0·7 (0·5–0·9)
	Men	0·8 (5/641)	0·6 (3/473)	2·1 (6/285)	3·2 (6/190)	3·9 (5/129)	4·5 (1/22)	—	
Italy Eight centres	Women	1·4 (8/568)	2·4 (13/538)	4·1 (22/541)	5·7 (31/542)	—	—	—	
	Men	1·2 (7/585)	1·8 (11/602)	5·3 (30/571)	7·0 (39/555)	—	—	—	1·3 (1·0–1·7)
The Netherlands Rotterdam	Women	0·9 (6/705)	1·3 (9/684)	3·7 (20/544)	5·6 (22/396)	6·9 (17/245)	4·4 (4/91)	10·0 (2/20)	Reference
	Men	0·8 (5/613)	2·1 (10/477)	2·9 (10/341)	5·6 (10/180)	5·1 (4/79)	4·5 (1/22)	—	
Spain Girona	Women	—	1·5 (5/328)	5·0 (13/256)	4·1 (7/170)	4·4 (4/90)	5·0 (1/20)	—	
	Men	—	0·4 (1/262)	4·0 (6/150)	2·6 (3/114)	6·7 (3/45)	—	—	1·0 (0·7–1·3)
Spain Pamplona	Women	—	1·3 (1/75)	3·8 (6/159)	2·0 (3/150)	3·6 (5/137)	6·8 (3/44)	—	
	Men	—	4·2 (3/71)	2·6 (4/152)	6·6 (10/152)	7·0 (10/142)	8·9 (4/45)	—	0·9 (0·6–1·3)
Total	Women	0·9 (18/1940)	1·6 (36/2281)	3·7 (75/2007)	4·5 (79/1754)	4·8 (39/812)	5·2 (14/268)	29·8 (10/48)	
	Men	0·9 (17/1839)	1·5 (28/1885)	3·7 (56/1499)	5·7 (68/1191)	5·6 (22/395)	6·7 (6/89)	—	

*Numbers in parentheses indicated the actual numerator and denominator.
†Dashes indicate age groups that were not included in the survey or for which prevalence estimates were not computed because of small numbers.
‡Prevalence estimates of the French study were weighted according to the sampling procedure; the denominators reported in the table were artificially computed by dividing the observed number of cases by the weighted prevalence.

unstable estimates due to small numbers. The likelihood ratio test was performed to test for heterogeneity across centres. To investigate whether age and sex adjusted prevalence figures of Parkinson's disease differed across studies, we calculated prevalence ratios and the corresponding 95% confidence intervals (95% CIs) by Poisson regression analyses with the Rotterdam study (the largest) as reference for comparison. We also used Poisson regression analysis to determine whether the overall age adjusted prevalence was significantly different between men and women.

Results

The overall study population comprised 17 205 elderly subjects, of whom 14 636 were 65 years of age and older (table 1). The response rates ranged from 68% in the survey from The Netherlands to 84% for the survey from Girona, Spain (table 1). Tables 3 and 4 and figs 1 and 2 show prevalence values and the prevalence ratios of parkinsonism and Parkinson's disease for the individual studies and overall. The overall age standardised prevalence (per 100 population) in subjects 65 years of age or older was 2·3 for parkinsonism

Table 4 Age and sex specific prevalence (per 100 population) of Parkinson's disease and overall age and sex adjusted prevalence ratios*

Population		Age group (y)†							Prevalence ratio (95% CI)
		65–69	70–74	75–79	80–84	85–89	90–94	95–99	
France Gironde‡	Women	0·2 (1/500)	0·2 (2/974)	1·8 (9/487)	1·0 (5/493)	2·2 (7/324)	1·9 (2/113)	7·1 (2/28)	
	Men	0·7 (4/556)	0·5 (2/399)	1·3 (4/308)	2·9 (5/173)	1·6 (2/125)	4·5 (1/22)	—	0·4 (0·3–0·6)
Italy Eight centres	Women	0·9 (5/568)	2·2 (12/538)	3·0 (16/541)	4·1 (22/542)	—	—	—	
	Men	0·5 (3/585)	1·0 (6/602)	3·7 (21/571)	5·0 (28/555)	—	—	—	1·2 (0·9–1·6)
The Netherlands Rotterdam	Women	0·6 (4/705)	1·0 (7/684)	2·4 (13/544)	4·8 (19/396)	5·3 (13/245)	3·3 (3/91)	5·0 (1/20)	Reference
	Men	0·8 (5/613)	1·7 (8/477)	2·3 (8/341)	3·9 (7/180)	3·8 (3/79)	— (0/22)	—	
Spain Girona	Women	—	1·5 (5/328)	4·7 (12/256)	3·5 (6/170)	4·4 (4/90)	5·0 (1/20)	—	
	Men	—	0·4 (1/262)	4·0 (6/150)	2·6 (3/114)	6·7 (3/45)	—	—	0·7 (0·5–1·1)
Spain Pamplona	Women	—	(0/75)	3·1 (5/159)	1·3 (2/150)	2·2 (3/137)	2·2 (1/44)	—	
	Men	—	1·4 (1/71)	1·3 (2/152)	4·6 (7/152)	4·9 (7/142)	2·2 (1/45)	—	1·1 (0·8–1·6)
Total	Women	0·6 (10/1773)	1·0 (26/2599)	2·8 (55/1987)	3·1 (54/1751)	3·4 (27/796)	2·6 (7/268)	6·3 (3/48)	
	Men	0·7 (12/1745)	1·0 (18/1811)	2·7 (41/1522)	4·3 (50/1174)	3·8 (15/391)	2·2 (2/89)	—	

*Numbers in parentheses indicate the actual numerator and denominator.
†Dashes indicate age groups that were not included in the survey or for which prevalence estimates were not computed because of small numbers.
‡Prevalence estimates of the French study were weighted according to the sampling procedure; the denominators reported in the table were artificially computed by dividing the observed number of cases by the weighted prevalence.

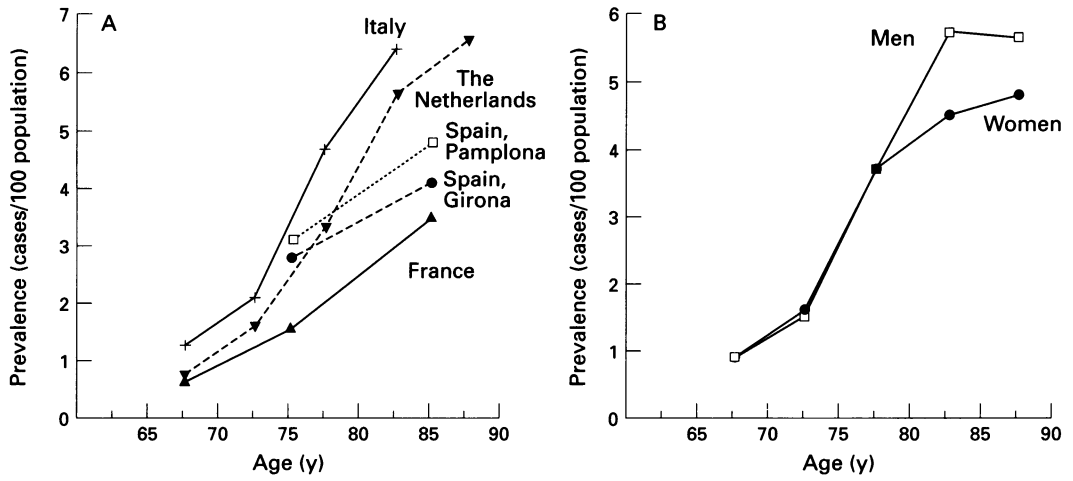

Figure 1 (A) Age specific prevalence, for both sexes combined, of parkinsonism in five European surveys. The prevalence estimates are plotted in the middle of the corresponding age groups: for the studies from Italy and The Netherlands by five year age groups, for the studies from France and Spain by 10 year age groups. (B) Overall age specific prevalence for women and men.

and 1·6 for Parkinson's disease. Prevalence figures of parkinsonism increased from 0·9 for those aged 65 to 69 years to 5·1 for those aged 85 to 89 years. The prevalence figures for Parkinson's disease increased from 0·6 for those aged 65 to 69 years to 3·5 for those aged 85 to 89 years. The prevalence of both parkinsonism and Parkinson's disease increased with age, after a similar pattern in all studies, with no decrease in extreme ages. After adjustment for age and sex, there were no significant differences across surveys except for the French study, in which prevalences were consistently lower. The likelihood ratio test showed heterogeneity across centres when the survey from France was included ($P < 0·001$). When the survey from France was excluded, there were no statistically significant differences across centres ($P = 0·21$). Figures 1 and 2 show the overall age and sex specific prevalences of parkinsonism and Parkinson's disease. The prevalences for men and women were not significantly different; for parkinsonism the women:men ratio was 0·96 (95% CI: 0·80–1·16), and for Parkinson's disease 0·94 (95% CI: 0·75–1·18).

The frequency distribution by type of parkinsonism for all studies combined was as follows: Parkinson's disease 68%, parkinsonism in dementia 9%, drug induced parkinsonism 5%, parkinsonism with associated features 1%, vascular parkinsonism 3%, and unspecified parkinsonism 14%. The proportion of subjects with Parkinson's disease who were newly diagnosed through the surveys varied from 11% in France and 13% in The Netherlands, to 26% in Girona, Spain, 31% in Italy, and 52% in Pamplona, Spain. In all surveys, the percentage of newly diagnosed patients with Parkinson's disease increased with age. For all studies combined, this percentage increased from 18% for those aged 65 to 70 years to 36% for those aged 80 to 85 years.

Discussion

METHODOLOGICAL CONSIDERATIONS

The striking variation in prevalence estimates of Parkinson's disease reported from various studies and different populations, ranging from 10 to 405 cases per 100 000 population,[1] may be caused, partly or completely, by variation in the methods used. The three most important methodological elements are the case finding strategy,[6] the diagnostic criteria for parkinsonism and Parkinson's disease, and the degree of coverage of the target population (response rate).

Studies that rely on existing medical records exclude from the prevalence estimate those patients who failed to seek medical attention for their symptoms, those who were incorrectly diagnosed, and those whose records

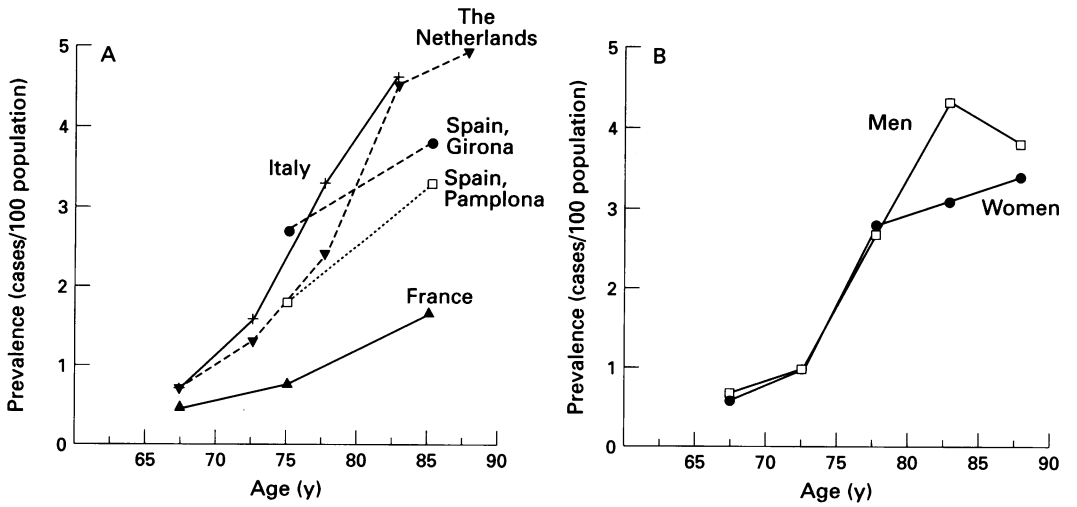

Figure 2 (A) Age specific prevalence, for both sexes combined, of Parkinson's disease in five European surveys. The prevalence estimates are plotted in the middle of the corresponding age groups: for the studies from Italy and The Netherlands by five year age groups, for the studies from France and Spain by 10 year age groups. (B) Overall age specific prevalence for women and men.

were not retrieved. The alternative case finding approach involves the direct or indirect contact of all subjects in the study population to assess their disease status. This approach should eliminate the underestimation of prevalence and should be more suitable for international comparisons as it reduces the variation due to differences in access to and quality of medical care in various populations.

Our study is the first comparison of results from several prevalence surveys of Parkinson's disease which used similar case finding strategy and diagnostic criteria. Although the five EUROPARKINSON surveys were not designed as a multicentre study, the investigators met and exchanged their methods and data collection instruments early in the planning of the surveys. Therefore, we have reached an unprecedented level of methodological homogeneity. To increase comparability across centres, the medical documentation of most parkinsonian patients underwent a centralised review by an adjudication panel.

Despite this effort to homogenise our methodology, the five surveys still present some variation. The screening procedures were different in number of items tested and personnel involved. In the French study, no physical examination was performed as part of the screening, whereas in the four remaining studies it was. Also, the use of diagnostic criteria for parkinsonism varied somewhat with a broadening of the criteria in the French study and a restriction in the Girona study. There were variations in the differential diagnosis of parkinsonism by specific aetiology. Parkinson's disease represented 70% to 96% of all parkinsonisms in Italy, The Netherlands, and Girona, Spain, whereas Parkinson's disease was only 59% of all parkinsonisms in Pamplona, Spain, and 48% in France. A large percentage of parkinsonian subjects in the French study had concurrent dementia with no clear time relation between onset of dementia and onset of extrapyramidal signs. These subjects were classified as "unspecified parkinsonism". In addition, a high percentage of subjects in France were receiving antidopaminergic agents, and were classified as "drug induced parkinsonism". It was again difficult in these patients to isolate the role of antidopaminergic drugs from the independent occurrence of Parkinson's disease.

In a two phase survey, failure to study a large segment of the target population (non-response) due to refusal or other obstacles may cause an underestimation or an overestimation of prevalence.[7] Unfortunately, the five surveys had different response rates, and the impact of this variation on our findings is unknown.

AGE

The prevalence of parkinsonism and Parkinson's disease increased with age in all five surveys for both men and women, with no decrease at higher ages. This suggests that the prevalence, and probably also the incidence, of Parkinson's disease continues to increase beyond the age 85 or 90 years. Various other surveys based on direct[6 8] or indirect[9 10] contact of all subjects in the population also showed a continuing increase in the prevalence of Parkinson's disease with age. By contrast, other prevalence studies based on existing medical records showed a peak in prevalence followed by a decline among the oldest old.[11–14] We speculate that these contrasting patterns are due to the underascertainment of Parkinson's disease among older subjects which occurs when patients are detected through medical records only. Our five surveys showed that the percentage of subjects with Parkinson's disease who had not been previously diagnosed increases with advancing age in the general population.

SEX

Most prevalence studies that indicated higher prevalences of Parkinson's disease in men[8 12 15–17] or in women,[11 14] were based on medical records, whereas most surveys with a personal screening for parkinsonism, such as our study, found no significant sex differences.[6 9 10 18] These findings suggest that the risk of Parkinson's disease is equal in men and women, but the referral to medical services varies by sex across populations.

GEOGRAPHIC COMPARISON

It has been postulated that geographic differences in the prevalence of Parkinson's disease may yield aetiological clues.[19–21] After adjusting for the effect of age and sex using Poisson regression models, our data did not suggest significant differences in prevalence across European countries, with the exception of the French survey. Morgante *et al* showed that a substantial proportion of parkinsonian subjects go undetected when only a questionnaire screening, as in the French survey, is used.[6] We think that the differences in methodology and in diagnostic criteria discussed may at least partly account for the lower prevalence estimates of Parkinson's disease in the French survey. Therefore, our overall impression is that there is no evidence for the prevalence of Parkinson's disease being different across European countries.

Although the overall prevalences were similar in our five surveys, there was a wide variation in the percentage of newly diagnosed patients with Parkinson's disease who were detected through the screening. This may be due to differences in referral pattern and in access to medical services across the four countries. These findings emphasise the importance of a direct screening when assessing the prevalence of Parkinson's disease.

Comparing our findings with those from other recent surveys based on a similar case finding approach, we found striking similarities with the Sicilian study.[6] This comparison strengthens our overall impression of limited geographic variation in prevalence when methods are homogeneous.

Some authors reported that persons living in a rural environment have a higher risk of developing Parkinson's disease than persons

living in towns, and suggested an environmental cause for Parkinson's disease.[18 22] In our study, the more rural population (Girona) or mixed populations (France, Italy) did not have a higher prevalence of Parkinson's disease than the more urban populations (Pamplona, Rotterdam).

Conclusions

To allow comparisons across countries, an effort was made in EUROPARKINSON to increase the homogeneity of case finding strategy and diagnostic criteria in five European surveys on the prevalence of Parkinson's disease. Allowing for the French study—which deviated somewhat from the common methods—our findings suggest that the prevalence of Parkinson's disease is similar across European countries. The prevalence of both parkinsonism and Parkinson's disease increases steeply with age, and is similar in men and women.

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List of all collaborators of EUROPARKINSON

France: JF Dartigues, F Tison, L Letenneur, P Henry *(Bordeaux)*; A Alpérovitch, C Tzourio, M Gautier *(Paris)*.

Italy: A Amaducci, M Baldereschi, D Inzitari, A Ghetti *(Florence)*; F Grigoletto, L Battistin, G Enzi *(Padova)*; A Capurso, P Livrea *(Bari)*; L Motta *(Catania)*; S Bonaiuto *(Fermo)*; C Loeb, C Gandolfo *(Genova)*; N Canal *(Milano)*; F Rengo *(Napoli)*.

The Netherlands *(Rotterdam)*: MMB Breteler, MC de Rijk, GA Graveland, A Ott, FGA van der Meché, A Hofman.

Spain *(Girona)*: S Lopez-Pousa, J Vilalta-Franck, J Llinás-Reglà, M Lozano-Gallego.

Spain *(Pamplona)*: JM Martínez-Lage, JM Manubens-Bertran, R Larumbe, J Muruzabal, P Martínez-Lage, C Guarch, T Urrutia, P Sarrasqueta, F Lacruz, P Quesada, C Lopez.

USA *(Rochester)*: WA Rocca.

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