

## Incidence and Risk Factors of Parkinson's Disease in The Netherlands

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**Abstract.** The incidence and some risk factors of Parkinson's disease were investigated in a study performed in The Netherlands. The study was based on a disease register of the Sentinel Stations, which provide a complete ascertainment of new patients with Parkinson's disease in 60 general practices in The Netherlands. The incidence rate of Parkinson's disease in The Netherlands is estimated to be 11/100,000 person-years for men and 12/100,000 person-years for women. Risk factors for Parkinson's disease were investigated in a case-control study in which 86 cases, with the diagnosis of Parkinson's disease confirmed by a neurologist, were compared with 172 reference subjects, matched for age and gender. Cigarette smoking was associated with a lower risk of Parkinson's disease (relative risk 0.6, 95% confidence interval 0.3-1.0). No association was observed between Parkinson's disease and severe head trauma with loss of consciousness, or surgery with total anaesthesia.

### Introduction

From 1981 to 1986, all new cases of Parkinson's disease occurring in 60 general practices in The Netherlands were registered. This provided the opportunity to study the incidence rate of Parkinson's disease, and to investigate risk factors for Parkinson's disease in a case-control study based on incident cases.

In this paper, we report the incidence rate of Parkinson's disease in The Netherlands from 1983 to 1985. We also report a study of

risk factors in 86 confirmed patients with Parkinson's disease and in 172 healthy reference subjects.

### Methods

In the Sentinel Practices of The Netherlands Institute for General Practice, all incident cases of Parkinson's disease were registered in 60 general practices in The Netherlands from 1981 to 1986. These general practices are located all over The Netherlands, and cover 1.2% of the Dutch population. They are considered to provide a good representation of the popula-

tion of The Netherlands in general demographic and socio-economic aspects [1]. In 1981, the total population covered by the Sentinel Practices included 80,049 men (1.1% of all Dutch men) and 83,528 women (1.2%).

#### Cases

In the period from January 1, 1981, to December 31, 1985, all patients with Parkinson's disease were registered. The general practitioners were asked to note all new patients with idiopathic Parkinson's disease, and to exclude patients with secondary parkinsonism from the register. In the present study, only cases of Parkinson's disease were included if the diagnosis, initially made by the general practitioner, was confirmed by further examination by a neurologist. A total of 123 confirmed cases were registered from 1981 to 1985; the annual numbers were 39, 33, 16, 13 and 22, respectively. Because of the possible inclusion of some prevalent cases in the early phase of the registration, we decided to base our incidence estimates on the last 3 years of the register (1983, 1984, 1985).

All 123 confirmed cases were eligible for the study of risk factors of Parkinson's disease. Of these 123 patients, 12 had died before we could reach them, 11 could not be reached and 12 refused to participate in the study. All other patients were asked to complete a mailed questionnaire. In 2 cases the questionnaire was returned but we were unable to use the data in the analysis. This left 86 patients with Parkinson's disease on which the risk factor study was based.

#### Controls

For each case, 2 healthy reference subjects from the same general practice, matched for age and gender, were invited to take part in the study. They were selected randomly (within the relevant 5-year age and gender group) from the population list of the general practitioner. The control subjects were asked to complete the same mailed questionnaire as the cases. Of the 172 reference subjects who were included in the analysis, 102 consented after a first selection, 54 after a second, 11 after a third and 5 after a fourth selection of reference subjects.

#### Data Collection

Information about putative risk factors for Parkinson's disease was obtained by mailed questionnaire. The questionnaire was the same for cases and controls, and included, besides questions on age, sex

and socio-economic status, specific questions about the history of cigarette smoking, severe head trauma and total anaesthesia. In general, the information on risk factors in both cases and controls was obtained within 6 months after the patient was entered into the register.

#### Data Analysis

The estimation of the incidence rate (incidence density) was based on the number of incident cases of Parkinson's disease in 1983-1985, divided by the number of person-years during those years in the 60 general practices.

The magnitude of the association of putative risk factors with Parkinson's disease was assessed by the odds ratio as an estimate of the relative risk (RR). The RR is presented with a 95% confidence interval (CI). The matching variables (age and gender) were taken into account by entering them into a model for logistic regression [2]. The reported adjusted RR are based on the regression coefficient yielded by this model. A separate matched-pair case-control analysis showed very similar results.

## Results

#### Incidence Rate

In table 1 the incidence rate of Parkinson's disease is presented per 100,000 person-years for men and women, separately. It is estimated to be 11/100,000 person-years for men and 12/100,000 for women.

#### Risk Factors

Table 2 presents the frequencies of cigarette smoking ever versus never for cases and controls. The adjusted RR amounted to 0.6 (95% CI 0.3-1.0). For smoking ever but not now versus never the adjusted RR was 0.5 (0.3-1.0). For smoking now versus never, the adjusted RR was 0.7 (0.4-1.4). A breakdown by gender yielded an adjusted RR of cigarette smoking ever versus never for men of 0.8 (0.4-2.0) and for women of 0.3 (0.0-0.9).

Table 1. Incidence rate of Parkinson's disease in The Netherlands per 100,000 person-years, 1983-1985

Year	Men	Women
1983	12 (9)	9 (7)
1984	6 (4)	12 (9)
1985	16 (11)	14 (11)
Total 1983-1985	11 (24)	12 (27)

Number of patients is indicated in parentheses.

Table 2. Cigarette smoking ever versus never

	Cases	Controls	Total
Smoking ever	31	82	113
Smoking never	55	90	145
Total	86	172	258

RR = 0.6 (95% CI 0.3-1.0); adjusted RR = 0.6 (0.3-1.0).

Surgery with total anaesthesia was not associated with the occurrence of Parkinson's disease. The adjusted RR amounted to 1.2 (0.6-2.0). For men this was 1.4 (0.6-3.8) and for women, 1.1 (0.4-3.0). A history of severe head trauma with loss of consciousness was not associated with Parkinson's disease. The adjusted RR was 1.4 (0.6-2.8).

These relationships of putative risk factors with Parkinson's disease were adjusted for potentially confounding variables, particularly of socio-economic status and education. The estimates of RR adjusted for these potential confounders did not differ materially from the ones presented above.

### Discussion

The main observations in this study are that the incidence rate of Parkinson's disease for men and women in The Netherlands is about 10/100,000 person-years, and that smoking of cigarettes appears to be associated with a halving of the risk of Parkinson's disease. These associations persisted after adjustment for measured confounding variables.

The finding of an incidence rate (incidence density) of 11 and 12/100,000 person-years in men and women, respectively, is in agreement with most previous reports [3-6; see ref. 7 for a review]. A study from Rochester, Minn., USA, reported considerably higher incidence rates, but in that study patients with drug-induced parkinsonism were included [8].

Our finding of a reduced risk of Parkinson's disease in smokers adds to the already extensive epidemiologic evidence [see ref. 9 for a review]. Our study has some advantages over earlier ones, in that it was registry-based, both in the selection of cases and controls, and that it was based on incident cases. These two features of the study design reduce the possibility of selection bias due to hospitalization or due to differential survival of smokers. We were not able to confirm a previous report [10] of an association of Parkinson's disease with head trauma.

In summary, these observations from a registry-based study of Parkinson's disease in The Netherlands provide confirmation for previously reported estimates of the incidence rate and of an inverse association with cigarette smoking.

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