

## Estimation of incidence and prevalence of Parkinson's disease in the elderly using pharmacy records

D. A. M. C. van de Vijver PharmD<sup>1\*</sup>, R. A. C. Roos PhD<sup>2</sup>, P. A. F. Jansen PhD<sup>3</sup>,  
A. J. Porsius PhD<sup>1</sup> and A. de Boer PhD<sup>1</sup>

<sup>1</sup>*Department of Pharmacoepidemiology and Pharmacotherapy, Utrecht University, Utrecht, the Netherlands*

<sup>2</sup>*Department of Neurology, Leiden University Medical Centre, Leiden, the Netherlands*

<sup>3</sup>*Department of Geriatric Medicine, University Medical Centre Utrecht, Utrecht, the Netherlands*

### SUMMARY

**Purpose** We determined the prevalence and incidence of Parkinson's disease among persons aged 55 years and older in pharmacy records.

**Methods** Data came from the PHARMO database which includes information on drug dispensing for all residents of six Dutch cities. We selected all persons aged 55 years and older who had used antiparkinsonian drugs, and calculated a chance for having Parkinson's disease with use of a previously validated logistic regression model. We used a cut-off of 0.5 (sensitivity 62%, positive predictive value 92%). Prevalence was estimated on the first Wednesday of October 1997, incidence on the first Wednesday of October 1993 until 1997. A patient was incident, if the first prescription for an antiparkinsonian drug was dispensed at least 180 days after entry into PHARMO. Prevalence and incidence were standardized to the Netherlands population of 1 January 1998. The prevalence was adjusted for the sensitivity and positive predictive value of the model.

**Results** The unadjusted prevalence (per 100 000) for those aged 55–64 years was 111, 65–74 years 598, 75–84 years 1551 and for persons aged 85 years and older 1847. The adjusted and standardized prevalence was 970 per 100 000 (95% confidence interval 869 to 1071). The incidence (per 100 000 person years) for persons aged 55–64 years was 12, 65–74 years 108, 75–84 years 257 and for persons aged 85 years and older 247. The standardized incidence was 109 per 100 000 person years (96 to 121).

**Conclusions** Prevalence and incidence were in range with the literature. Pharmacy records therefore seem to be a useful tool for continuous monitoring of incidence and prevalence of Parkinson's disease. Copyright © 2001 John Wiley & Sons, Ltd.

**KEY WORDS**—incidence; prevalence; Parkinson's disease; antiparkinsonian drugs; pharmacy records; logistic regression model; levodopa; selegiline; pharmacoepidemiology

### INTRODUCTION

Epidemiological studies have shown that Parkinson's disease is a relatively common disease among the

elderly.<sup>1</sup> With the substantial increase in longevity of the population worldwide, there is a growing need to continuously monitor the incidence and prevalence of Parkinson's disease. The most reliable method for frequency estimation of the disease is a door-to-door survey, in which an entire population is screened for the disease using the same diagnostic criteria.<sup>2–5</sup> However, such an approach is expensive and time-consuming, especially for obtaining an incidence rate.<sup>5,6</sup>

Pharmacy records are a reliable source of true drug exposure.<sup>7,8</sup> They offer an easy and inexpensive

\*Correspondence to: David van de Vijver, Utrecht University, Department of Pharmacoepidemiology and Pharmacotherapy, PO Box 80082, 3508 TB Utrecht, The Netherlands. Tel: +31 30 253 67 19. E-mail: d.a.m.c.vandevijver@pharm.uu.nl

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way to collect drug exposure information for a large number of patients during a number of years. Antiparkinsonian drugs are a reliable marker for Parkinson's disease among persons aged 55 years and older in pharmacy records.<sup>9</sup> Pharmacy records can therefore be used to monitor the occurrence of Parkinson's disease.

The aim of the present study was to determine the prevalence and incidence of Parkinson's disease among patients aged 55 years and older in pharmacy records with use of a logistic regression model.<sup>9</sup>

## METHODS

### Data

Data were obtained from the PHARMO system, which includes information on drug dispensing and linked hospital discharge records for all 300 000 residents of six Dutch cities from 1991 to 1998.<sup>10</sup> For this study we used the data from 1993 onwards.

### Patients

From the PHARMO database, we selected all patients that were at least 55 years of age and who used antiparkinsonian drugs. The antiparkinsonian drugs were amantadine, anticholinergic drugs (biperidene, dexetimide, orphenadrine, procyclidine, trihexifenidyl), dopamine agonists (bromocriptine, lisuride, pergolide, ropinirole, pramipexole), levodopa, and selegiline. Parkinson's disease was predicted through a stepwise multivariate logistic regression formula.<sup>11</sup> The coefficients of the formula were obtained using data from the Rotterdam Study, which screened a whole population aged 55 years or older for the disease. Diagnostic criteria of the Rotterdam Study can be read elsewhere.<sup>3</sup> For each antiparkinsonian drug user we calculated a chance for having Parkinson's disease through a logistic regression model.<sup>9</sup>

$$e^x / (1 + e^x)$$

where:  $x = -13.054 + 0.10 * \text{age} + 6.08 * \text{amantadine} + 3.76 * \text{anticholinergics} + 5.62 * \text{dopamine agonist} + 6.51 * \text{levodopa} + 13.22 * \text{selegiline}$ .

Users of a certain antiparkinsonian drug were given a value of 1, patients who did not use that drug were given a value of zero. A patient for whom a value of 0.5 or more was calculated through the model was assumed to have Parkinson's disease. At a value of 0.5 the model determines Parkinson's disease with a sensitivity of 62.2%, a positive predictive value of

92.0%, and a specificity of 99.9%.<sup>9</sup> Excluded were patients for whom Parkinson's disease was determined but who used anticholinergics as the only antiparkinsonian drug during the study period and who used these drugs together with antipsychotics. These patients were assumed to have drug-induced parkinsonism. It was assessed whether the model determined Parkinson's disease correctly in PHARMO. All patients aged 55 years and older with a hospital discharge diagnosis of Parkinson's disease, which are the only available records in which the disease is explicitly stated in PHARMO, were selected. Subsequently, we excluded all patients who had not filled a prescription after the day of discharge. It was then determined what proportion of patients was identified within 4 days after discharge by use of the model, as having Parkinson's disease. According to Dutch law, during the study period patients were allowed to take medicines from a hospital supply for a few days and then had to retrieve their medication from a community pharmacy.

### Analysis

For our prevalence estimate we used the first Wednesday of October 1997. This day was chosen to exclude possible influences of weekends and holidays on the filling of prescriptions. The prevalence rate was standardized<sup>12</sup> to the Netherlands population of 1 January 1998 with 95% confidence intervals (CI 95%) using a binomial distribution.<sup>13</sup> The size of the population was obtained from the Dutch central bureau of statistics (CBS). As we have stated before, the sensitivity of the model was 62.2%. The reason that this sensitivity was not higher was because not all patients with Parkinson's disease receive antiparkinsonian drugs (yet).<sup>9</sup> We multiplied the prevalence rate by 1.48 (i.e. the model's positive predictive value divided by the sensitivity), to control for patients that were not treated with antiparkinsonian drugs.

A person was incident with Parkinson's disease when predicted through the model for the first time on any first Wednesday of October from 1993 until 1997. Furthermore, the first prescription for an antiparkinsonian drug had to be received at least 180 days later than the first dispensing date in PHARMO. The number of incident patients was divided by the number of person-years in the PHARMO area during 1993 to 1997. The incidence rate was not adjusted for sensitivity and positive predictive value, because we assumed that all patients with Parkinson's disease would eventually receive antiparkinsonian drugs.

The incidence rate was standardized<sup>12</sup> to the Netherlands population of 1 January 1998 with CI 95% using a Poisson distribution.<sup>13</sup>

## RESULTS

In the PHARMO database, 140 patients had a discharge diagnosis of Parkinson's disease and filled a prescription after discharge. The model predicted that 133 of these patients (95%) had Parkinson's disease.

A total of 493 persons were using antiparkinsonian drugs on the first Wednesday of October 1997. For 355 patients a value of at 0.5 or higher was calculated. One patient used anticholinergics for treatment of antipsychotic-induced parkinsonism and was thus excluded. Therefore, 354 patients had Parkinson's disease. These patients used the following antiparkinsonian drugs: 303 persons used levodopa (86%), 106 selegiline (30%), 87 dopamine agonists (25%), 45 anticholinergics (13%), and 33 persons used amantadine (9%). The summarized percentages exceeded 100%, because combinations of different antiparkinsonian drugs were used.

The crude prevalence rate (per 100 000) was 636 (CI 95% 570–702). After standardization, the rate increased to 658 (CI 95% 588–724). Adjusting for patients with Parkinson's disease that were not treated with antiparkinsonian drugs, the prevalence rate was 970 (CI 95% 869–1071). Figure 1 shows that the prevalence per 10-year age category increased with age in both men and women.

Our prevalence rate is higher than the estimates calculated using medical records (Table 1). The prevalence estimate corrected for patients who are not being treated with antiparkinsonian drugs resembles the rates found in door-to-door surveys.

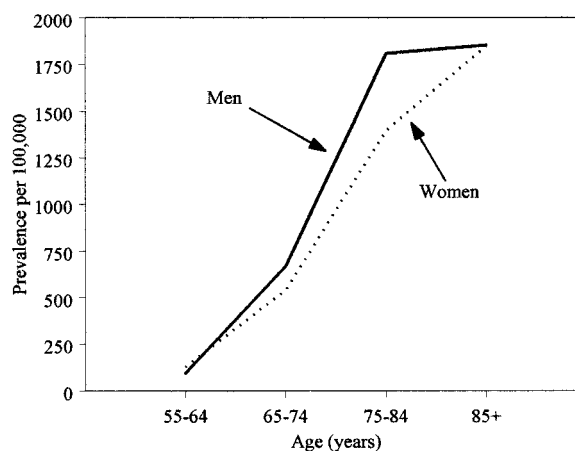


Figure 1. Prevalence of Parkinson's disease among women and men by age category

During follow-up, 278 new patients were found to have Parkinson's disease. Three persons were assumed to have antipsychotic-induced parkinsonism and were therefore excluded. This left 275 incident patients. The following antiparkinsonian drugs were used by incident patients: 132 used levodopa (48%), 99 selegiline (36%), 35 amantadine (13%), 12 anticholinergics (4%), and eight patients used a dopamine agonist (3%).

The crude incidence rate (per 100 000 person-years) over the 1993 until 1997 period was 102 (95% CI 90–113). The standardized incidence rate was 109 (95% CI 96–121). Figure 2 shows that the incidence rate among men increased with age. The rate among women reached a maximum at the age category 75 until 84 years. The incidence rate among men was higher in all 10-year age categories.

Table 1. Comparison of prevalence of Parkinson's disease among people aged 55–60 years or older estimated in this study and prevalences reported in the literature (all prevalences are adjusted to the Netherlands population of 1 January 1998)

Place	Type*	Year	Prevalence per 100 000	
			55 + years	60 + years
Aberdeen <sup>22</sup>	2	1984	601	
Cossato <sup>21</sup>	2, 3			553
Ferrara <sup>23</sup>	2	1988		508
Junín <sup>4</sup>	1	1991	1392	
Northampton <sup>24</sup>	2	1992		559
Rotterdam <sup>3</sup>	1	1991–1993	1306	
Sicily <sup>2</sup>	1	1987		1389
This study	3	1995	658 (970) <sup>†</sup>	822 (1216) <sup>†</sup>

\*Type of case ascertainment: 1, door-to-door survey; 2, medical records; 3, pharmacy records.

<sup>†</sup>Estimates corrected for patients with Parkinson's disease who are not being treated with antiparkinsonian drugs.

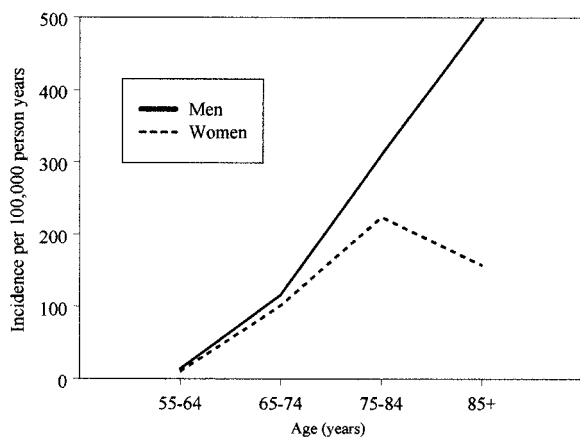


Figure 2. Incidence of Parkinson's disease per 100 000 person-years for women and men by sex and 10-year age category

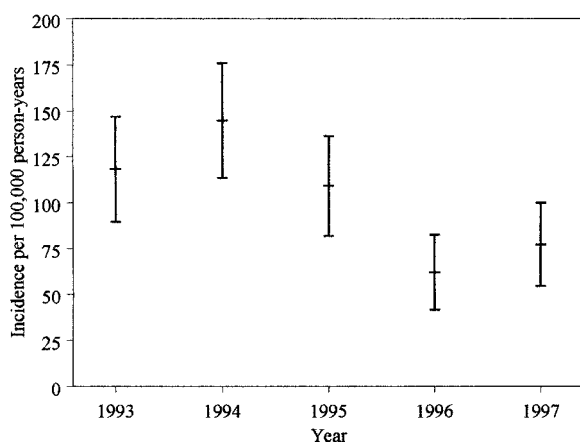


Figure 3. Variation of incidence rate of Parkinson's disease and its 95% confidence interval per calendar year

Table 2. Comparison of incidence of Parkinson's disease among people aged 55–60 years or older estimated in this study and incidences reported in literature (all incidences are adjusted to the Netherlands population of 1 January 1998)

	Place Type*	Years	Incidence per 100 000 person-years	
			55+years	60+years
Rotterdam <sup>6</sup>	1	1993–1995	213	
Ferrara <sup>23</sup>	2	1967–1987	27	
Hawaii <sup>†25</sup>	2	1965–1994	57	
Iceland <sup>26</sup>	2	1954–1963		102
Olmsted County <sup>27</sup>	2	1976–1990		68
Östergötland <sup>28</sup>	2	1986–1988		44
Turku <sup>29</sup>	2	1968–1970		68
Italy <sup>5</sup>	1	1992–1996		331 <sup>‡</sup>
This Study	3	1991–1995	109	133

\*1, door-to-door survey; 2, medical records; 3, pharmacy records.

<sup>†</sup>Only male persons.

<sup>‡</sup>65 years and older.

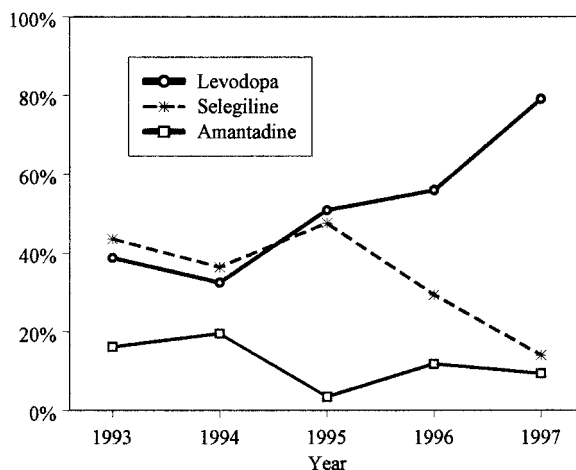


Figure 4. Proportion of incident users of antiparkinsonian drugs per calendar-year. Dopamine agonists and anticholinergics are not presented, because there were too few users per year

A variation in incidence per calendar year was found (Figure 3). Years in which a greater proportion of patients was incident on selegiline show a higher overall incidence (Figure 4). Our incidence estimate is comparable to studies based on medical records that included secondary forms of parkinsonism. (Table 2) The estimate is, however, lower than rates found in door-to-door surveys.

## DISCUSSION

We found an increase in the prevalence of Parkinson's disease with age. Our prevalence estimate was slightly higher compared to previous rates based on medical records. After correcting for patients with Parkinson's

disease that were not treated with antiparkinsonian drugs, the prevalence estimate was more comparable to rates found in door-to-door surveys. The incidence showed an increase with age in men. In women, the rate dropped in the oldest age category. The incidence estimate was lower than rates found in door-to-door surveys, and higher than figures based on medical records. Of all patients for whom a hospital discharge diagnosis for Parkinson's disease was found, 95% were identified as having the disease by this model. This means that virtually all patients with Parkinson's disease at discharge diagnosis were identified. However, it is expected that these patients had more severe forms of Parkinson's disease and were therefore more likely to receive antiparkinsonian drugs.

In this study a correction factor was used to control for patients with Parkinson's disease that were not treated with antiparkinsonian drugs. This factor was based on a population that was entirely screened for the disease.<sup>3</sup> Although this population was different from that used in the present study, we expect that the correction factor is a good approximation, because both populations are comparable regarding health care system and the way community pharmacies process prescription data. A more precise estimation of disease frequency can be obtained through a door-to-door survey, but this is expensive and time consuming. Door-to-door surveys are therefore less applicable for continuous monitoring of incidence and prevalence.

We found a variation in the incidence rate in time: higher estimates were found in years with a higher proportion of incident selegiline users. In these years, selegiline was thought to have neuroprotective properties and thus slow down progression of disease.<sup>14</sup> Doctors therefore prescribed selegiline as soon as possible in newly diagnosed patients. Incident use of selegiline declined after 1995, because it was reported to increase mortality risk.<sup>15</sup> At the time that this increased risk was disputed,<sup>16,17</sup> the supposed neuroprotective effect of selegiline was not found in a large placebo-controlled double-blind randomized trial.<sup>18,19</sup>

Previous studies have used pharmacy records to estimate prevalence of Parkinson's disease.<sup>20,21</sup> De Pedro-Cuesta and Rosenqvist used levodopa sales,<sup>20</sup> which is an unreliable method since identification of diseased individuals is impossible. Chio *et al.* did not compare their results with a population that was entirely screened for the disease and could therefore not correct for patients that were not treated with antiparkinsonian drugs.<sup>21</sup> Both studies used levodopa as the only tracer for PD, although other antiparkinsonian drugs can also be used.<sup>9</sup> The uncorrected preva-

lence rate in our study is slightly higher than estimates obtained in medical records,<sup>21-24</sup> but lower than rates found in door-to-door surveys.<sup>2-4</sup> In a door-to-door survey every individual of a population is screened for the disease. All patients, including those that have not come to medical attention (yet), will thus be identified. Medical records will only identify patients who did visit a physician with their parkinsonian complaints. These patients are more likely to use antiparkinsonian drugs. The rates obtained in medical records are therefore more comparable with our uncorrected estimate.

Our incidence rate is higher than incidence measures found in medical records<sup>23,25-29</sup> and lower than rates found in door-to-door surveys.<sup>5,6</sup> Medical records probably found lower rates for two reasons. First, selegiline was not used as extensively during the time the medical records estimates were obtained. Therefore, doctors might have preferred to delay initiation of treatment to minimize the risk of developing motor fluctuations that are associated with long-term use of antiparkinsonian drugs.<sup>30</sup> It is therefore likely that the proportion of incident patients that are not treated with antiparkinsonian drugs yet, is smaller in our study compared to the reports based on medical records. Second, incidence has been reported to vary by region.<sup>1</sup>

The literature is not consistent with respect to the increase of incidence with age. Some reported a drop in the rate at higher ages,<sup>23,26,27,29</sup> whereas others found that incidence increased with age.<sup>5,25,28</sup> These inconsistencies may be due to the difficulties in finding the oldest incident patients with Parkinson's disease: they may have died, or moved to nursing homes.

In conclusion, prevalence increased among the elderly with age. Incidence increased with age among men, and dropped in the highest age category among women. Our study presents pharmacy records as a tool for a fast and cheap estimation of incidence and

#### KEY POINTS

- Pharmacy records are presented for a cheap and fast estimation of Parkinson's disease, and thus for continuous monitoring of the frequency of disease
- Prevalence increased with age among men and women
- Incidence increased with age among men. The incidence estimate for women reached a maximum for the age category 75 to 84 years

prevalence of Parkinson's disease in the elderly. Pharmacy records can be used for continuous monitoring of Parkinson's disease.

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