# Parkinson's Disease: Time, Place, Person and Survival

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Parkinson's disease (PD) is a neurodegenerative disease mainly affecting the ageing brain. As an increasing number of people nowadays survive into old age, neurodegenerative diseases place a growing demand on health care resources. Various studies on the epidemiology of PD have been conducted worldwide. The important starting point for most epidemiological investigations is a descriptive study to give a useful initial overview of the condition under study. Two main measures of descriptive studies to quantify the burden of a disease in a population are disease frequency and distribution. The latter encompasses three categories: time, place and person. This article reviews the updated data of the distribution of PD and survival.

## Distribution of Disease

### Time

#### Secular trends

Time trends in the incidence of PD may lead to generating new etiologic hypotheses and they also have an impact for public health. A few studies were conducted in the same country, but the methodologies used were different. Some studies found a decrease in prevalence and incidence[1], whilst others reported no significant change[2] or even an inverse association (increase).[3] Explanations for these findings may be derived from the changes in the age structure of the population, different case finding procedures, and revisions of diagnostic criteria.

#### Periodic change (seasonality)

Two small-scale studies reported a slightly increased PD risk for persons born in the months of January, February, and March, whereas another study of larger sample size showed this association for persons born in winter and early spring only. Though the mechanism is unclear, one study suggested that the influenza pandemic could have led to an increase in risk of developing PD. A Canadian study investigated this relationship and found neither systematic seasonal variations in PD incidence nor seasonal variations in the severity of PD signs and symptoms.[4,5]

### Place

#### Broad geographical difference

As aforementioned, the major problem in comparing studies across countries are the differing time periods of conduct as well as age and gender patterns of the study populations. Both the long course of the disease and the increase in life expectancy have contributed to an increase in PD prevalence worldwide with large variations between countries. Not every investigation used age standardisation and, therefore, the comparison of prevalence and incidence measures unlikely represents the true variation of the disease.

#### Local difference: rural and urban environment

Several studies provided evidence to suggest a higher prevalence of PD in rural areas as compared to urban areas[3,6,7], whereas the findings of other studies[8,9] did not lend support this observation. Environmental exposures (i.e. pesticides or drinking water) may explain this difference. The proportion of newly undiagnosed PD cases was found to be higher in rural areas compared to urban areas (91% vs. 57%) and also higher in developing countries.[10] Reasons for this disparity may be the restricted access to specialist medical services and the difficulty of diagnosing the condition, particularly mild forms and in very old individuals.

### Person

#### Age

Case ascertainment in older people may be inaccurate due to the high incidence of subtle extrapyramidal signs on neurological examination with unknown neurological or psychiatric disease. The incidence of PD rises sharply after the age of 60. Age-specific incidence increased from approximately 11 to 20 per 100,000 person-years between the ages of 45 and 64 to 116 to 181 per 100,000 person-years for persons aged 85 years or over.[11,12] Age is not only associated with the increase in PD incidence, but it may also contribute to the difference in clinical presentations. Patients with late-onset PD have greater motor impairment than patients with middle-age onset.[13] This might result from the more

rapid disease progression, less aggressive or less potent medical treatment, or influences of co-morbid illnesses.

### Gender

The incidence rate of PD is higher in men compared to women especially in the older population. Between the ages 50 to 59 years, the male:female ratio for annual incidence of PD is 1.3. This ratio rises to 2.7 at the ages of 80 to 89 years.[14] By average, the male:female ratios of PD incidence ranged from 1.5 to 2. Oestrogen may protect neuronal cell death through its antioxidant properties. However, some studies did not support this difference.[15-17] Figure 1 illustrates the age-adjusted male:female ratios for incidence of PD.

### Ethnic group

Epidemiologic data show that the prevalence of PD is higher in whites than in Hispanics, blacks or Asians.[12] However, this issue remains controversial. A study in northern Manhattan revealed the highest incidence rate of PD in blacks compared to whites and Asians, which contradicted most studies estimating PD prevalence.[12] A study in northern California showed that the age- and gender-adjusted incidence rate was highest among Hispanics, followed by non-Hispanic whites, Asians and blacks.[14] The possible explanations of this discrepancy might be the variation in population characteristics, case definitions, methods of case ascertainment, sources of PD cases, and denominator populations. A Singaporean study shows the similar age-adjusted prevalence of PD among Chinese, Malaysians, and Indians in Singapore.[21] However, the participation rate of this study was 64% and there was the discrepancy between the proportion of population and the participation rate.

### Family (genetics)

Familial PD comprises about 10% of PD cases.[17] In young onset PD, there is a higher chance for a genetic component. In twin studies, which used positron emission tomography (PET) scans to detect pre-symptomatic cases, there was a significant three-fold higher concordance rate for monozygotic twins compared to dizygotic twins. Also, pedigree analysis from Swedish family studies suggested an autosomal dominant inheritant pattern with male predominance. Monogenetic PD forms from several gene mutations (PARK1-11) display atypical clinical pictures from sporadic PD.

### Occupation and socioeconomic group

The epidemiologic data of the association between socioeconomic factors and PD are inconsistent. Educational level was reported to be positively and negatively correlated with PD risk.[22,23] Many epidemiologic studies examined the association between occupations and PD risk, which are summarized in Table 1. However, the data are controversial. Most of the studies on occupational risk factors were case-control studies. They were, therefore, subject to methodological limitations.

### Survival

Before the introduction of the treatment with levodopa, Hoehn and Yahr reported a shorter survival in PD with the mortality ratio of 2.9.[28] In the early phase of the introduction of levodopa, there were several studies which showed a reduction in mortality and some even reported that patients treated with levodopa had the same mortality pattern as general population.[18,29,30] However, most recent post-levodopa era have reported a relative risk for death of PD of 1.5 to 2.5 (Table 2).[31-33] The leading cause of death is pneumonia.[34] Mortality was higher in patients who were older, had a higher Unified Parkinson's Disease Rating Scale score and Hoehn and Yahr staging, poor response to levodopa and dementia.[33,35,36] The mean duration of the disease until death is 9 to 12.5 years.[15,31,35,37] PD is associated with an approximately 8-year decrease in life expectancy.[38]

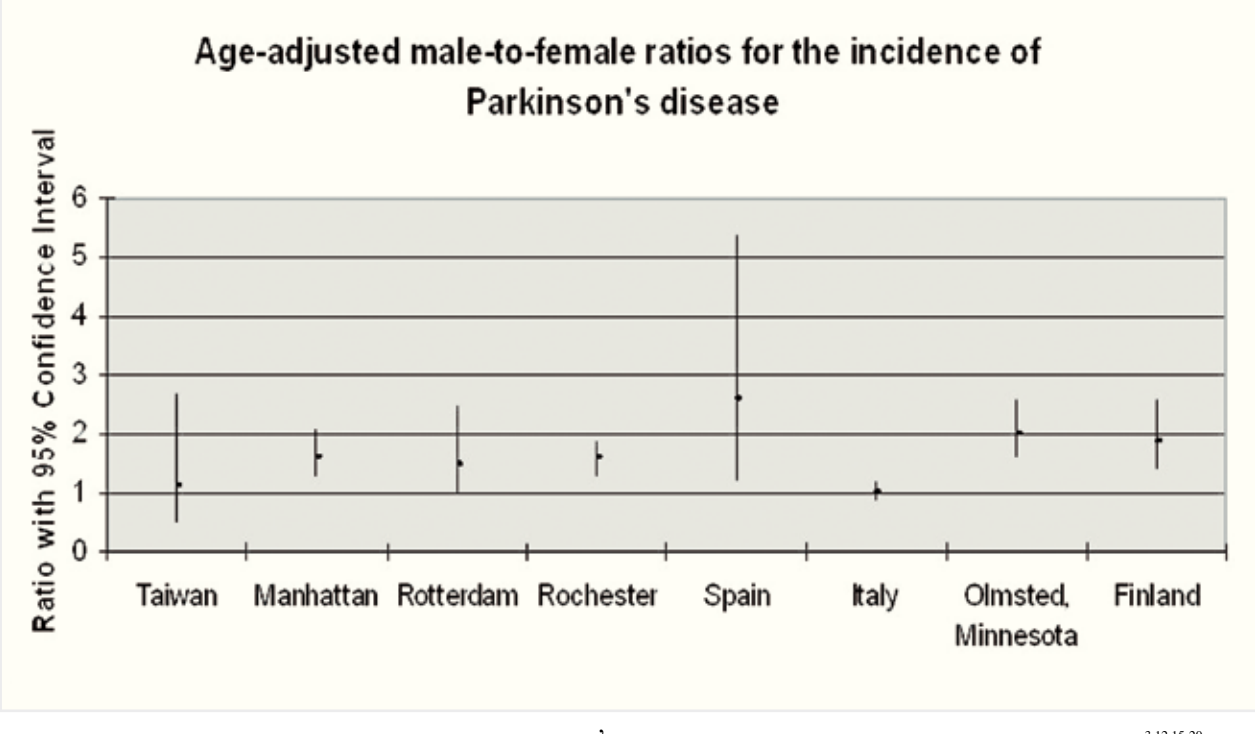



**Fig 1.** Age-adjusted male:female incidence ratios of Parkinson's disease with 95% confidence intervals from 8 studies.[3,12,15-20]

**TABLE 1.** Results of studies of occupational risk factor for Parkinson's disease.

| Study | Increase risk | Decrease risk |
|---|---|---|
| Olmsted, Minnesota[23] | Physician | Construction and extractive workers (e.g., miners, oil well drillers), production workers (e.g., machine operators, fabricators), metal workers, and engineers |
| Sweden[24] | Agricultural work along with pesticide exposure, male carpenters and female cleaners | |
| Greater Vancouver[25] | Teaching and occupation in healthcare services | |
| South Korea[26] | Agriculture, hunting and forestry; subcategory agriculture, production crops | Transportation; subcategory transporting and driver Technicians; subcategory metal, machinery and related engineers |
| Italy[27] | Farming, well water use | |

**TABLE 2.** Mortality ratios in Parkinson's disease.

| Study | PD cases | Relative risk of death | 95% Confidence Interval |
|---|---|---|---|
| Sicilian neuroepidemiologic study[32] | 59 | 2.3 | 1.6-3.4 |
| Norway[33] | 245 | 1.5 | 1.3-1.8 |
| Health professional follow-up study[39] | 288 (men) | 1.6 | 1.3-2.0 |
| Olmsted, Minnesota[37] | 196 | 1.6 | 1.2-2.1 |
| DATATOP database[36] | 800 | 1.0 | 0.9-1.2 |
| Sydney[31] | 130 | 1.6 | 1.2-2.0 |
| Italy[34] | 59 | 2.1 | 1.4-3.1 |
| Taiwan[15] | 15 | 3.4 | 2.1-4.3 |

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