

A Systematic Review of the Worldwide Prevalence and Incidence of Parkinson's Disease

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Background: A number of epidemiologic studies of Parkinson's disease (PD) have been conducted worldwide over the years. Although every study reported the rise in prevalence and incidence rate of PD with the increasing age, the overall estimates were different across countries. The variation in reported data may partly be contributed by case ascertainment, case finding method, data collection, and most importantly different population structures.

Objective: Systematically review prevalence and incidence of PD and find the causes of variation in the results.

Material and Method: A literature search was conducted on Medline and EMBASE for studies worldwide investigating the prevalence and incidence of PD and included all adults, English and publication between 1965 and January 2010. The primary search of both databases yielded 5,330 results. After screening topics and abstracts, 168 relevant abstracts were tagged and saved for more thorough perusal. Ultimately, 40 papers were selected for review after applying the pre-specified inclusion criteria

Results: The worldwide prevalence of PD varies widely. One reason for the variation in prevalence estimates could be due to the differences in survival across countries. The use of epidemiological studies using medical records could be another reason for the variation in disease frequency.

Conclusion: PD is common in the elderly. A number of descriptive epidemiologic studies have been conducted worldwide. Comparing the incidence and prevalence of Parkinson's disease is difficult.

Keywords: Parkinson's disease, Parkinsonism, Epidemiology, Prevalence, Incidence

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Parkinson's disease (PD) is the second most common neurodegenerative disorder after Alzheimer's disease⁽¹⁾. PD leads to disability and affects quality of life⁽²⁾. In addition, it puts considerable emotional stress and economic burden on caregivers⁽²⁾. The spectrum of disease comprises of movement disorders and non-motor symptoms like dementia, depression, visual hallucination and autonomic dysfunction⁽³⁾. Several epidemiologic studies conducted worldwide over the years have found varying rates of disease burden⁽⁴⁻¹¹⁾. The present study reviewed the worldwide prevalence

and incidence of PD and the reasons for the variation in disease frequency.

Case ascertainment

Clinical diagnosis

The two commonly used diagnostic criteria are: (1) presence of two or more of the following cardinal signs, resting tremor, rigidity, postural instability and gait difficulty, (2) UK Brain Bank Criteria. This criterion has been used in recent studies to increase the accuracy of case ascertainment.

Secondary causes of Parkinsonism and Parkinson plus syndrome must be excluded before a diagnosis of PD can be confirmed. Ideally, the diagnosis should be confirmed by a neurologist or movement disorder specialist since the diagnostic error rate in a general practice setting is close to 50%⁽¹²⁾.

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The positive predictive value of clinical diagnosis of PD by neurologists associated with the movement disorders service was as high as 98.6% with the sensitivity of 91.1%⁽¹³⁾.

Neuro-imaging in PD

The use of advanced neuroimaging techniques in the evaluation of PD is known to increase the reliability of disease ascertainment⁽¹⁴⁾. (18F) fluoro-dopa positron emission tomography (PET) and single-photon emission computed tomography (SPECT) can assess nigrostriatal dopaminergic function in PD patients⁽¹⁵⁾. However, it is not feasible to use neuro-imaging in population-based epidemiological studies.

Pathological diagnosis

Although clinical criteria and neuroimaging can give a diagnosis of probable PD, the definitive diagnosis of PD requires histological confirmation through postmortem examination⁽¹⁶⁾. A study by Hughes et al observed that postmortem histological examination could confirm the clinical diagnosis of idiopathic PD made by specialists in 76% of case⁽¹⁷⁾. In addition, the retrospective application of the UK Brain Bank criteria improved the diagnosis accuracy to 82%^(17,18).

Methodology

Literature search

A literature search was conducted on Medline and EMBASE for studies worldwide investigating the prevalence and incidence of PD. The MeSH keywords used for the search were “Parkinson”, “Parkinson’s disease”, “Epidemiology”, “Incidence” and “Prevalence”. Search limits included Human, All adults, English and publication from 1965 through January 2010. A search of the citations of included papers and published relevant reviews was also performed. One problem with conducting a literature search on worldwide PD studies was that there were many such articles, due to the long history of PD research. Therefore, strict inclusion criteria were applied to ensure that the articles retrieved would be of a high standard. The general inclusion criteria were: (1) publication in English, (2) study population larger than 3000 participants for population-based survey studies, unless they were the only study of a country (for registry-based studies, a denominator of more than 20,000 participants was required to ensure that the number of cases was sufficient and that the estimates were statistically precise), (3) the diagnostic criteria

used for case ascertainment were explicit, (4) the age-specific rate was reported, to ensure that the prevalence and incidence rates could be comparable. The primary search of both databases yielded 5,330 results. After screening topics and abstracts, 168 relevant abstracts were tagged and saved for more thorough perusal. Ultimately, 40 papers were selected for review after applying the pre-specified inclusion criteria. Supplementary Table 1 and 2 (available as Supplementary Data on the journal’s website) show the reported prevalence and incidence rates.

Disease Frequency

Prevalence

The worldwide prevalence of PD varies widely. Several reasons could be attributed to this variation. One reason for the variation in prevalence estimates could be due to the differences in survival across countries. The use of epidemiological studies using medical records could be another reason for the variation in disease frequency. These studies may not be generalisable to the population since it excludes individuals with subclinical disease who were unlikely to seek medical care. This could be observed from the fact that a number of studies using 2-phase door-to-door surveys identified undiagnosed PD in the population from 12% to 69%^(9,19-22). Fig. 1 describes the prevalence of PD based on door-to-door survey and Fig. 2 describes the prevalence based on epidemiological studies using hospital records. Overall, the standardized prevalence (all ages) per 100,000 in door-to-door surveys ranged from 57 to 230. This is higher than the prevalence observed with

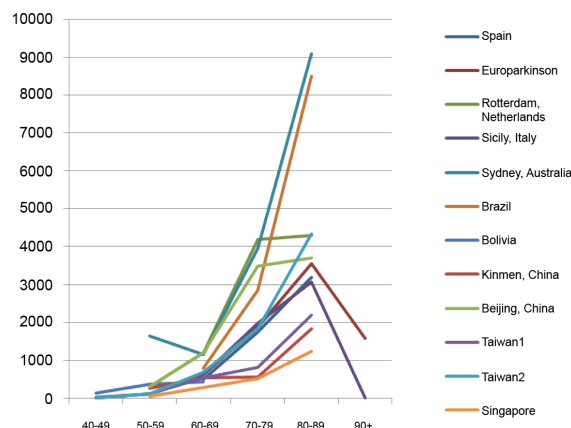


Fig. 1 Age-specific prevalence of Parkinson’s disease from door-to-door surveys^(8,10,19,20,22-29)

record-based studies. The increase of PD prevalence with age can be observed across the world although the absolute numbers differ.

Incidence

Quantifying the incidence of PD has been more difficult because of the issues of case ascertainment, different inclusion, and exclusion criteria, one single point in time of case assessment and the lack of histological confirmation. Most incidence reports published in the literature were from record-based epidemiological studies. Most of the studies reported crude incidence rate 10 to 13 per 100,000 person-years and age-adjusted incidence rate of 7.9 to 19 per 100,000 person-years. Fig. 3 and 4 show age-specific incidence rates from epidemiological studies using door-to-door surveys and studies using medical records, respectively. The mean age of symptom onset was 62 to 70 years and was rare before age 50 years. The peak incidence was between 70 to 79 years. Several studies also showed a decreased incidence in the population aged more than 80 years. However, a door-to-door survey showed that the majority of undiagnosed PD patients were aged 80 years or older⁽⁹⁾. Therefore, this apparent low incidence rate in the very old individuals, may be due to underdiagnosis, restricted access to health services, and difficulty in disease diagnosis due to the presence of other co-morbid conditions. Moreover, the incidence rate in the very old may be simply because of the instability of estimates based on small numbers of cases in this age group.

Proportion of Parkinson's disease compared to other types of Parkinsonism

Parkinsonism can be classified into idiopathic (PD), secondary and Parkinson plus syndrome. The proportion of PD is shown in Fig. 5. By average, PD comprised 63% (range 42-86) of Parkinsonism.

Hoehn and Yahr stage distribution

The estimated prevalence by disease stage (Hoehn and Yahr classification) from eight studies is shown in Fig. 6. The proportion of each stage in each study is different. In most of the studies, more than 50% of PD cases were in stage I or II^(8,9,22,50).

Methodological challenges

1. The diagnosis of PD mainly relies on clinical presentations. The neurological examination is often difficult especially in the very old. Extrapyramidal

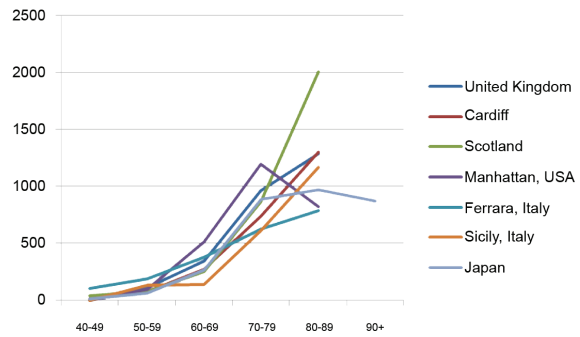


Fig. 2 Age-specific prevalence of Parkinson's disease from record-based studies⁽³⁰⁻³⁶⁾

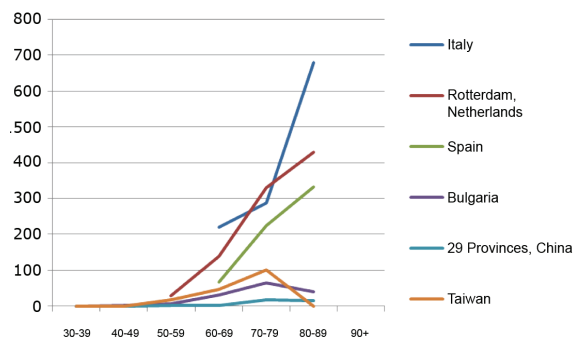


Fig. 3 Age-specific incidence rate of Parkinson's disease from door-to-door surveys^(4,8,37-40)

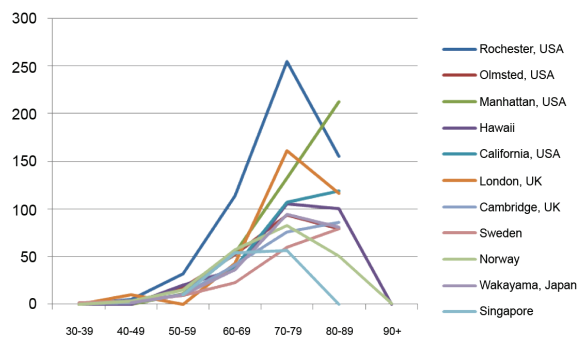


Fig. 4 Age-specific incidence rate of Parkinson's disease from record-based surveys^(6,33,41-49)

signs may be age-related, making it difficult to separate early Parkinsonism from normal ageing. A study looking at the diagnostic accuracy of PD from general practices showed that the diagnosis of clinically probable PD was confirmed in 53% of presumed PD cases⁽¹²⁾. For the accuracy of case ascertainment in

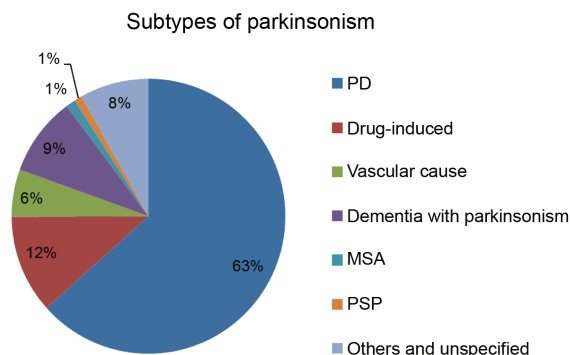


Fig. 5 Subtypes of parkinsonism from pooled data of 12 studies (2,716 patients)^(6,10,20,22,23,25,27-30,35,37,38,48,49)

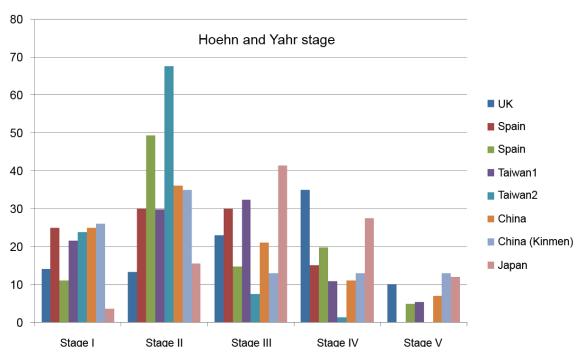


Fig. 6 The distribution of 761 Parkinson's disease patients according to the Hoehn and Yahr classification^(8,9,22,26,29,32,36,50)

the epidemiologic data, the diagnosis should ideally been confirmed by a neurologist which is usually impractical in real practice. Moreover, the incidence rate in the very old may be simply because of the instability of estimates based on small numbers of cases in this age group.

2. As described before, the different diagnostic criteria used in case ascertainment influenced prevalence estimates. Therefore, surveys using different diagnostic criteria cannot be used for comparison. In addition, these studies used different inclusion and exclusion criteria. Earlier studies tended to use less specific criteria than more recent studies. Stricter criteria yield higher specificity with the cost of lower sensitivity and broader criteria yield the opposite.

3. Self-reporting of PD status was proposed to be a screening tool to identify patients for epidemiologic study. However, it yielded lower precision for diagnosis than clinical assessment with a clinical

pathologic correlation in 40% of cases⁽⁵¹⁾. Moreover, the criteria used in diagnosis cannot be identified in these studies. Therefore, it was not included in this study. Likewise, studies using drug prescription alone as a case finding method are not included as they underestimate mild cases that do not need medication, and they may misclassify cases with other diagnosis that use medication for other indications.

4. Any study that uses patient assessment in a single period may not be accurate⁽⁵²⁾. The diagnosis of early PD is difficult and sometimes needs the long-term follow-up to see response to dopaminergic therapy, disease progression and the development of any features suggestive of Parkinson plus syndrome⁽⁵³⁾. On the contrary, patients with diagnosis of drug-induced Parkinsonism may actually have concomitant PD. The diagnosis of PD then can only be identified after the offending drugs are ceased and patients are further assessed. One study reported the false positive rate of 8% and false negative rate of 9% detected on the second examination two months after the preliminary diagnosis⁽²¹⁾. However, the long-term follow-up is time consuming and expensive. This may be impractical in population-based studies.

5. Case finding methods varied from hospital-based record, door-to-door survey and self-report. Even in the door-to-door survey, there were still variety in techniques used such as one-stage and two-stage survey, instruments used, identified informants and interviewers. These differences definitely affected the outcome of the studies.

6. Record-based studies may underestimate incidence and prevalence, especially in the countries with restricted access to health care. Moreover, the distribution of PD may be distorted, as there might be more atypical cases (*i.e.* young-onset) than the general population.

7. As a community-based study, participation rate is essential to be reported. People who did not participate might have Parkinsonism, which limited them to join the studies, or they may be the group with low prevalence of PD. The studies with a low participation rate can therefore be imprecise.

8. Though PD is a common neurodegenerative disease, it is still uncommon in the population compared to many other diseases. Therefore, a large sample size is always needed to yield statistically precise estimates. The small number of cases can give an imprecise rate and wide confidence interval.

9. The prevalence of PD is influenced by the incidence and duration of illness. The gender difference

in PD in the different age groups might simply reflect difference in survival once PD has developed and difference in life expectancy.

Conclusion and Recommendation

PD is common in the elderly. A number of descriptive epidemiologic studies have been conducted worldwide. However, the lack of well-designed and large-scale studies was the limitation in the past. Comparing the incidence and prevalence of Parkinson's disease is difficult. Varying methodologies, different diagnostic criteria and case finding strategies contribute to the variation in the reported prevalence and incidence of PD. Ideally, a large prospective, long term follow-up study, 2-phase door-to-door survey, the same diagnostic criteria used, participants examined by specialists and being assessed more than once, same age strata used and data standardized to reference population are potential factors to make more comparable and precise estimates. Future direction may also need to identify pre-asymptomatic period, proteomics, environmental and genetic factors that will lead to the success in disease prevention and treatment.

Key points

1. The prevalence and incidence of PD increase with the increasing age.
2. Four common causes of Parkinsonism were PD, drug-induced Parkinsonism, dementia with Parkinsonism and vascular Parkinsonism.
3. Door-to-door surveys demonstrated higher disease frequencies than record-based surveys.
4. Varying study methodologies and differing case ascertainment methods were the most important reasons for the reported variation in incidence and prevalence of PD.

Potential conflicts of interest

None.

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การทบทวนวรรณกรรมอย่างเป็นระบบเรื่องความชุกและอุบัติการณ์ของโรคพาร์กินสันทั่วโลก

วิรัชศักดิ์ เมืองไพศาล, อาจุ แมทธิว, ฮิโรยูกิ ฮอริ, เดวิด ซีเดล

ในระยะเวลาที่ผ่านมาได้มีการศึกษาทั่วโลกถึงระบาดวิทยาของโรคพาร์กินสัน ถึงแม้ว่าทุกการศึกษาได้รายงานถึงการเพิ่มขึ้นของความชุกและอุบัติการณ์ของโรคพาร์กินสันเนื่องจากอายุขัยของประชากรเพิ่มมากขึ้น แต่การประมาณการของตัวเลขที่รายงานยังแตกต่างกันไปในแต่ละประเทศ ความแตกต่างของข้อมูลที่รายงานอาจเกิดจากวิธีการวินิจฉัยโรค วิธีในการค้นหาผู้ป่วย วิธีในการเก็บข้อมูล และสิ่งที่สำคัญคือ ความแตกต่างของโครงสร้างของประชากร จุดมุ่งหมายของบทความนี้ คือ การทบทวนรายงานความชุกและอุบัติการณ์ของโรคพาร์กินสันอย่างเป็นระบบ และการพยายามอธิบายถึงสาเหตุของความแตกต่างในการรายงานผลการศึกษานี้