



**parkinson's
australia**

National Advocacy • Connection • Awareness

Ecosystem of Parkinson's in Australia Project

prepared by Professor George D. Mellick
for Parkinson's Australia, January 2024

Part 2: Systematic Review

Parkinson's Australia is registered as a Public Benevolent Institution with the
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Executive Summary

As the national advocate for the Australian Parkinson's community, Parkinson's Australia prioritises the need to work with our stakeholders to raise national awareness of Parkinson's, educate and empower the community about Parkinson's and ultimately create better outcomes for all those impacted by Parkinson's in Australia. To achieve these goals there is a need to the best possible evidence base to support our advocacy.

The Board of Parkinson's Australia commissioned the Ecosystem of Parkinson's in Australia Project with the aim to gather the best available information about the current impact of Parkinson's in Australia, to identify critical gaps in the available evidence base and to recommend, where needed, potential new directions of investigation that might enable this information to be collected and disseminated.

The project is multifaceted and ongoing. It is intended that various parts of the project would be released as individual report documents addressing specific issues. Ultimately Parkinson's Australia hopes that the Ecosystem Project will promote better community awareness, advocacy and connection, and reduce the burden of Parkinson's in Australia.



G.Mellick@griffith.edu.au

Griffith Institute
for Drug Discovery
Nathan, QLD 4111

Parkinson's Facts

Parkinson's is the second-most common neurological condition in the world, but remains one of the least understood.



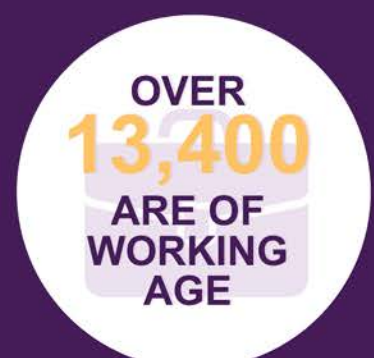
52% are
male



48% are
female



Cost to economy
>**\$10** billion p/a



Part Two

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1. Part two summary

Reporting the numbers of individuals living with a condition at any time (prevalence) and the numbers who develop a condition over a set time-period (incidence) are important measures crucial to understanding the condition, providing clues about risk factors and enabling resource planning and provision.

This paper provides a review of the international literature around how incidence and prevalence of Parkinson's disease (PD) can be measured and provides a summary of the studies in Australia to-date. There are no primary data on Australian incidence figures, but crude estimates based on pooled international incidence figures reveal that 41 per 100,000 people develop PD each year. This suggests that 10,660 people developed PD in Australia in 2022. Seven primary Australian prevalence studies have produced widely different estimates; however, the average of these reveals that 496 per 100,000 people live with PD (or 128,960 Australians in 2022).

Crude pooled international data produce a prevalence figure of 315 per 100,000, which equates to 121,200 Australians in 2022. Very limited information exists regarding the geographic distribution of incidence and prevalence. This review re-enforces the sensitivity of estimates to methodological differences and highlights the critical importance that population structure (especially age and sex distribution) plays in the estimates. It suggests that using age and sex-stratified data from meta-analysed international data is a more nuanced way to model the incidence and prevalence of PD in Australia to provide baseline information of geographic distribution and potential changes over time.

PART TWO

Ecosystem of Parkinson's in Australia Project

2. Introduction

The Incidence & Prevalence of Parkinson's Disease: A Review with an Australian Focus

What is parkinsonism and Parkinson's disease?

Parkinson's disease (PD) is a complex neurodegenerative condition that leads to a multitude of medical symptoms across many health domains with a significant impact on the quality of life of those who are affected. First reported in the Western Medical literature by Dr James Parkinson in his 1817 "*Essay on the Shaking Palsy*" (Parkinson, 2002), the entity popularised as *Maladie de Parkinson* by the famous French neurologist Charcot in the late 19th Century (Lees, 2007).

The cluster of motor symptoms which make up the salient features of Parkinsonism, namely tremor, rigidity and slowness of movement (akinesia and bradykinesia) which are often accompanied by postural instability, result from the disruption of specific neurological pathways that make up the nigrostriatal tract within the mid-brain. There are many reasons why this tract within the brain may be defective. Hence there are many causes of the symptoms of Parkinsonism. However, the chronic and selective degeneration of specific dopamine producing neurons within a region of the brain known as the Substantia Nigra together with the deposition of proteaceous inclusions in the brain containing a protein, alpha-synuclein, leads to a pathological diagnosis of Primary or Idiopathic Parkinson's disease (iPD).

Diagnosing Parkinson's

The distinction between Primary Parkinson's disease and Secondary Parkinsonism Syndromes (including other neurodegenerative diseases termed Parkinson's Plus Syndromes) can be made clinically by specialist physicians but diagnostic certainly can sometimes be difficult. There are no specific tests for Parkinson's disease. In life, the diagnosis is largely based on history, examination and the exclusion of signs and symptoms of an alternative diagnosis. Definitive diagnosis requires pathological confirmation at autopsy.

Idiopathic (meaning of unknown cause) Parkinson's disease is a progressive condition, insidious in onset and chronic in trajectory. For many years considered primarily as a movement disorder, PD is now recognised for its many and various non-motor signs and symptoms, including cognitive, neuropsychiatric, autonomic, gastrointestinal and others (Martinez-Martin & Ray Chaudhuri, 2018). This reflects the importance of the multiple body systems involved and the more generalised nature of the condition.

Causes & risk factors

There are likely to be many specific triggers of the neurodegenerative process that occurs in PD; hence there are many causes. However, it is clear that the process is complex and a combination of multiple environmental, genetic and age-related factors are in play (Figure 1).

Age is the most significant risk factor for Parkinson's with most cases developing over the age of 60. However, there is still a significant number who develop symptoms in early adulthood and there are even cases of juvenile onset (before the age of 20).

Other confirmed factors that increase risk include family history of PD, environmental toxin exposure and male sex; while cigarette smoking has been shown to reduce risk.

Many commonly occurring genetic variables are associated with a modified risk – although the effect sizes are very small and when looked at individually are clinically insignificant. Risk factor analysis provides important clues to assist in understanding the determinants of the condition.

Causes & risk factors continued

One valuable way to examine differential risk is to look for differences in disease incidence across disparate groups. However, this is methodologically very difficult and, for reasons discussed below, most attempts to do this for Parkinson's have been thwarted by methodological challenges and the dominating factors associated with population structure (namely differences in the distribution of age and sex, two of the most significant determinants of Parkinson's incidence).

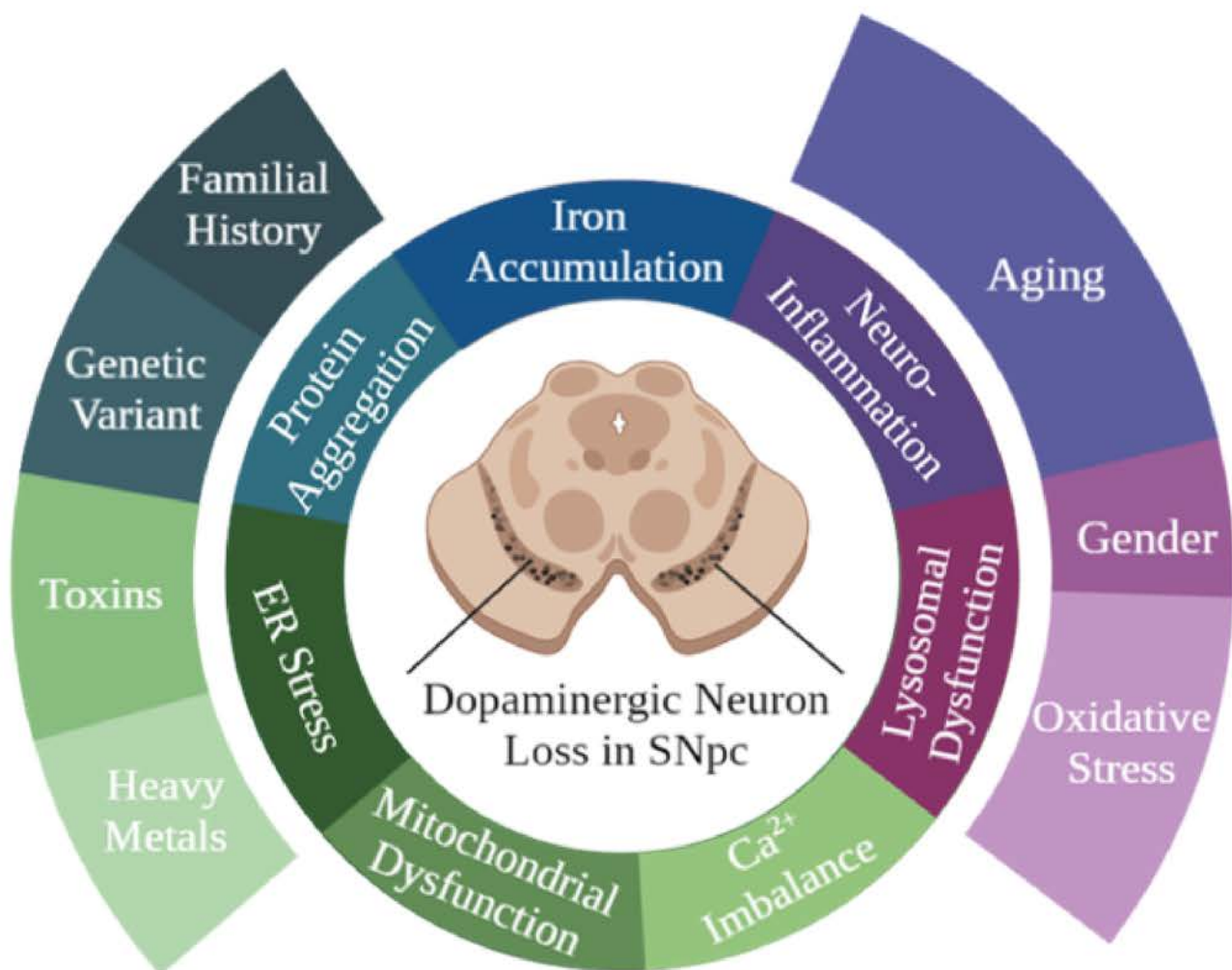


FIGURE 1. Risk factors and pathological features of Parkinson's disease.
(picture adapted from Chen et al. 2023)

3. Defining incidence & prevalence

The incidence of a condition refers to the number of new cases occurring over a specific period of time (for example over one year). Prevalence refers to the number of cases existing at a specific point in time. Prevalence is not only dependent on incidence but is also influenced by survival and remission. For Parkinson's disease, which currently has no cure and is thus no remission, prevalence depends on survival.

Many studies have reported on the incidence and prevalence of Parkinson's disease in the literature. There have been several systematic reviews of this literature that aim to summarise the information and identify salient points that need to be considered when interpreting these data (Hirsch et al., 2016; Pringsheim et al., 2014).

There have been relatively few primary studies of the incidence and prevalence of Parkinson's in Australia. A 2013 article presented all previous attempts up to that year, highlighting the sparsity of this information and the need for further investigations (Mellick, 2013).

In 2023, a comprehensive systematic review of the Australian literature by Fealy and colleagues confirmed this gap in published work, re-enforced the importance to further investigate the incidence and prevalence at different geographical locations, and reiterated that vastly different figures have previously emerged from published studies (Fealy et al., 2023).

4. Methods to assess incidence & prevalence

There are several legitimate ways to estimate the incidence and prevalence of a condition like Parkinson's disease. These are summarised in Table 1. The well-established gold-standard is the door-to-door survey which samples an entire well-defined population (or representative samples thereof) and comprehensively investigates everyone for the symptoms. Often for Parkinson's this is done using a two-tiered approach where an initial screen for symptoms of Parkinsonism is followed by formal neurological examination by training physicians using strict diagnostic criteria. While this is the most rigorous and well-validated method, it is expensive, logistically complex and difficult to perform across large population areas.

Methods utilising health and medication usage records can be valuable, especially across entire systems or jurisdictions, although these methods introduce several biases and limitations, not least of which is the fact that the undiagnosed are excluded a particular problem for Parkinson's where up to 24% identified in door-to-door surveys have been previously undiagnosed (de Rijk et al., 1997).

Recently, Australian epidemiologists, trying to tackle the challenges of estimating the prevalence of dementia, have suggested that a combined approach might form a reasonable compromise. This methodology, known as "Capture-Recapture" uses data-linkage of administrative databases combined with targeted research (Flicker et al., 2022; Waller et al., 2017). This approach has not been attempted for Parkinson's disease in Australia or elsewhere, to date.

Assessing incidence and prevalence

Table 1. Methods to gather incidence and prevalence data on Parkinson's

Method	Comments
Medical records	Excludes undiagnosed and mis-diagnosed.
Analysing medication usage	Multiple confounders including culturally-determined prescribing practices, health system access issues and drugs used for different indications.
Door-to-door survey / Random sampling	Gold Standard but expensive and logistically difficult. Emerging privacy issues.
Population-based surveys	Low response rate; consent difficult.
Capture-recapture data linkages	A new combined approach.

5. Systematic review of the literature

In order to review all the relevant recent international literature in the area of Parkinson's disease incidence and prevalence, an extensive literature search was undertaken. The details of the search methodology are presented in Figure 2. The initial search identified two comprehensive systematic reviews and meta-analyses published on incidence (Hirsch et al., 2016) and prevalence (Pringsheim et al., 2014). The initial search strategy was supplemented by secondary searches using the identical search strategies described in these reviews (but restricting the date of publication from 2013 to present) and also by examining all papers that have cited either of these reviews. This methodology is considered to comprehensively cover all legitimate peer-reviewed studies that have examined this issue over the past decade.



Search strategy for systematic review of incidence and prevalence

Identification

Records identified through initial PubMed database searches using terms: "parkinson disease"[MeSH Terms] AND ("epidemiology" [MeSH Subheading] OR "epidemiology" [All Fields] OR "prevalence"[All Fields] OR "prevalence"[MeSH Terms] or "prevalence s"[All Fields] OR "prevalent"[all fields]) AND 2013/01/01:3000/12/31[Date - Publication] (n=4,977)

Records identified using identical search strategy as that reported in previous systematic reviews published by Pringsheim et al. (2014) and Hirsh et al. (2016) (limiting publication date from 2013-present) (n=6,274)

Screening

Records screened in total (after removing duplicates) (n=8,825)

All articles that cite Pringsheim et al. (2014) or Hirsh et al. (2016) (n=1,419)

Titles/Abstracts screened (after removing duplicates) (n=313)

Articles with Australian content (n=3)

Eligible and included

Full-text articles screened (included and considered in review) (n=313)

MODIFIED PRISMA FLOW DIAGRAM

6. Results

The results from this comprehensive search of the literature largely confirm the findings previously presented by Pringsheim and colleagues (Pringsheim et al., 2014) and Hirsch et al (Hirsch et al., 2016). These highlight that door-to-door surveys using a two-tiered methodology remain the gold standard. They also suggest that when age and sex distribution is controlled for, the overall incidence and prevalence of PD is relatively consistent across different groups of people. Thus, comparisons between populations and across time are extremely sensitive to changes in demographics and these considerations are paramount in data interpretation.

The findings across this literature confirms that prevalence and incidence estimates are largely dependent on population structure and fine-grain analysis of sub-groups. Many of the primary sources of research do not consider important differences in age and sex distributions of the populations in which the estimates are being taken. While some investigations of geographic distributions may provide some interesting clues, these studies are not usually designed in a way that enables good quality comparisons once methodological differences are taken into consideration. It is important not to place too high an emphasis on interpretation of these figures, particularly if population structures are not appropriately controlled for. This is also particularly relevant when trying to determine how incidence and prevalence changes with time. To adequately do this, it is critical to also consider how the overall population structure has evolved over the time periods concerned.

Interestingly, the reviews produced by Pringsheim and Hirsch provided criteria with which to judge the quality of estimates of the studies included in their meta-analyses. They included those studies which fulfilled requirements that took age and sex distributions into consideration with the knowledge that these factors are among the most significant drivers of differences in incidence and prevalence. The other factor that contributes greatly to the variability in results is the diagnostic criteria for Parkinson's and Parkinsonism used in such studies. The accepted gold-standard clinical diagnosis of Parkinson's is made by a movement disorders neurologist, although this can only be confirmed with 100% accuracy at autopsy. This means that different forms of Parkinsonism may be misdiagnosed in certain situations. These issues make it challenging to directly compare studies in different populations that use inconsistent diagnostic criteria.

The meta-analysed incidence and prevalence results presented in the Hirsch and colleagues (Hirsch et al., 2016) and Pringsheim and colleagues (Pringsheim et al., 2014) studies are summarised in Table 2 and Table 3 for incidence and prevalence, respectively.

Pooled age & gender-specific incidence (per 100,000 per year)

Table 2. Results from the meta-analysis of gender-specific incidence of Parkinson's disease published and adapted from Hirsch and colleagues (Hirsch et al., 2016).

Age Group	Female	95% CI	Male	95% CI
40-49	2.94	0.95 - 9.09	3.59	0.70 - 18.39
50-59	13.40	6.77 - 26.51	19.68	7.31 - 52.97
60-69	58.53	37.05 - 92.45	55.10	15.88 - 191.22
70-79	104.99	81.15 - 135.84	132.72	81.99 - 214.86
80+	66.02	48.43 - 90.00	110.48	78.56 - 155.38

**Overall 41 per 100,000
per year**

Pooled age & gender-specific incidence (per 100,000)

Table 3. Results from the meta-analysis of gender-specific prevalence of Parkinson's disease published and adapted from Pringsheim and colleagues (Pringsheim et al., 2014).

Age Group	Female	95% CI	Male	95% CI
40-49	45	18 - 113	36	15 - 86
50-59	41	24 - 71	134	63 - 285
60-69	392	202 - 762	389	211 - 715
70-79	813	433 - 1,524	932	494 - 1,757
80+	1,517	840 - 2,740	2,101	918 - 4,809

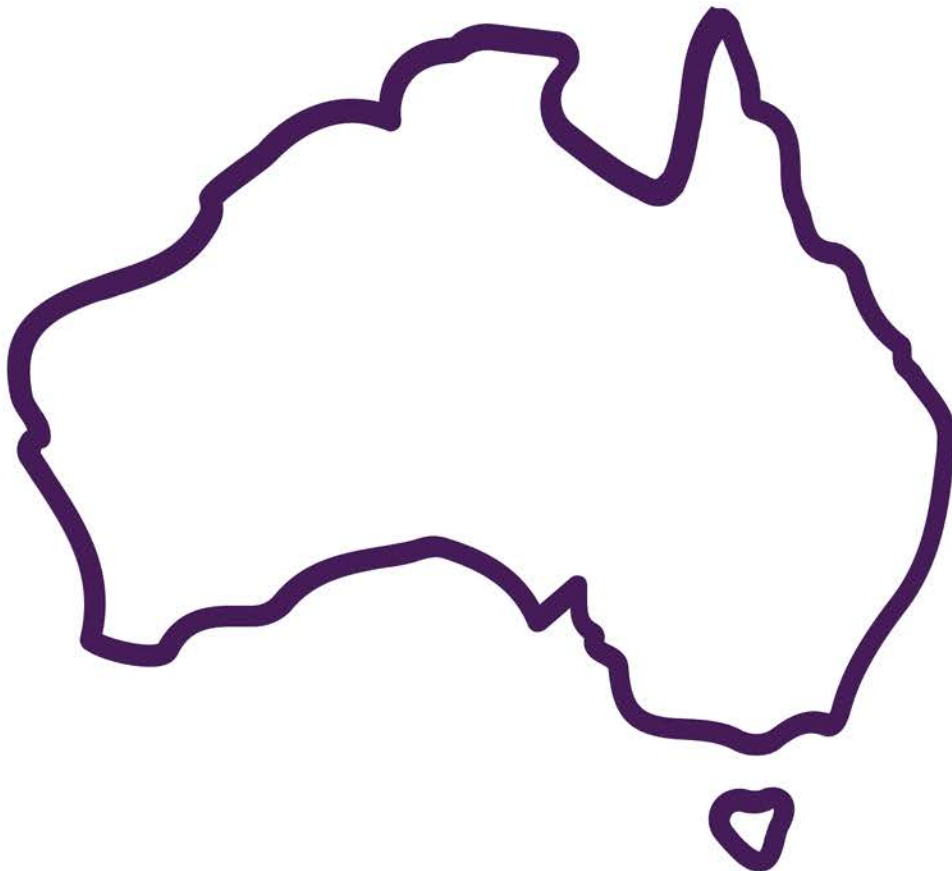
Overall 315 per 100,000

In an Australian context

In an Australian context, there have been no studies providing data on PD incidence. However, using the pooled meta-data from Hirst and colleagues we can make an initial crude estimate of incidence. Based on the 2022 population of Australia from the ABS (26 million), this crude incidence of PD is estimated to be around 10,660 individuals.

Similarly, very few primary studies report Australian prevalence figures. A summary of these studies is presented in Table 4. The vast difference in the reported prevalence estimates relates to differences in methodology, particularly ascertainment methods and study populations (Mellick, 2013).

The data have been reported as crude prevalence per 100,000 of the population (not corrected for population differences in age and sex). Also, notably there are extremely wide confidence intervals which emerge for several reasons including sampling frame and sample size.



Australian publications

Table 4 Published prevalence estimates from Australian studies adapted from (Mellick, 2013). Note that studies 3 (Chan et al., 2001) and 4 (Chan et al., 2005) only reported cases over the age of 55 and study 6 (Mehta et al., 2007) reported cases over the age of 49.

Study	Method	Prevalence per 100,000 (95% CI)
1. Jenkins, 1996	GP Survey (Gippsland, VIC)	66 (95% CI: not available)
2. McCann et al., 1998	Cross-sectional (Nambour, QLD)	414 (95% CI: 53 - 775)
3. Chan et al., 2001	Door-to-door survey (Randwick, NSW)	776 (95% CI: 452 - 1,241)
4. Chan et al., 2005	Door-to-door survey (Bankstown, NSW)	775 (95% CI: 467 - 1,209)
5. Peters et al., 2006	GP survey (Queensland State-wide)	146 (95% CI: 136 - 1,241)
6. Mehta et al., 2007	Cross-sectional (Blue Mountains, NSW)	446 (95% CI: 279 - 774)
7. Ayton et al., 2019	PBS prescription data in Victoria	850 (95% CI: 210 - 1,490)

Average 496 per 100,000

Further details of these studies can be found in the published articles by Mellick (Mellick, 2013) and Fealy and colleagues (Fealy et al., 2023). While not statistically robust, it is interesting to note that the average of all these Australian estimates (Table 2) is 496 per 100,000 which, based on an Australian population of 26 million people in 2022, equates to 128,960 people living with PD in Australia. In comparison, using the pooled meta-data from the Pringsheim study we can make an initial crude estimate of 2022 prevalence of PD in Australia to be 121,200.

As noted in the publication by Ayton and colleagues mentioned above (Ayton et al., 2019), recent efforts have been made to use medication prescription data to provide estimates of PD prevalence. The current literature review yielded an interesting Australian paper that discussed the prescribing of Parkinson's medications in Australia, highlighting the fact that around half of those receiving a prescription for such medications have not got the diagnosis of PD (Koponen et al., 2022). This paper provides some details as to how to control appropriately for this and identify the bono fide patients in this group. The publication by Ayton and co-workers from Victoria (Ayton et al., 2019) from which it appears some claims about national prevalence have recently been made, has some potential limitations that may not have been fully considered. Firstly, their case ascertainment, done on the basis of single medication prescriptions, leads to excessive over-estimation of prevalence. Secondly, their study looking at regional differences does not fully consider population substructure, but instead tries to statistically control for demographic co-variables in a regression analysis. This analysis concluded that rurality was not associated with increased prevalence but did claim an association between pulse farming in the local government area and increased prevalence of Parkinson's (Ayton et al., 2019). Using the criteria set by Pringsheim (Pringsheim et al., 2014) the Ayton study would not have been given a high enough quality score to be included in their analysis.

While there have been a few attempts to look at differences in prevalence and incidence on the basis of geographic location, ethnic background, or other subgroup analyses, most differences could be explained away once population demographics or other methodological issues with respect to case ascertainment, diagnostic criteria and other factors were taken into consideration (Hirsch et al., 2016; Pringsheim et al., 2014).

In Australia, previous reports from the Australian Institute of Health and Welfare have highlighted inequities in the provision of health care in general and in health outcomes for those living outside of urban centers in Australia . Anecdotally, these inequities extend to those living with PD. This is supported by published studies that suggest that health related quality of life of PLWP is poorer (Soh et al., 2012) and the availability, quality and consistency of PD-related health care service provision is considerably more variable for those outside metropolitan areas (Duncan & Rositano, 2011). To attempt to address these inequities, it is critical to determine clear and defensible data regarding incidence and prevalence numbers in different geographical areas of Australia.

The systematic review of Fealy and colleagues concluded that two of the Australian studies provided hints that PD may be more prevalent in regional, rural and remote Australia compared to urban areas (Ayton et al., 2019; Peters et al., 2006); however, methodological limitations in these analyses necessitate that these clues to be followed-up with better designed studies. Moreover, as there is very sparse baseline data from which to make comparison, this information is desperately required to inform future examinations of this issue. To obtain these data, it is possible to use the age-and gender stratified incidence and prevalence data provided in the meta-analyses of high quality published international studies and to use these figures in conjunction with well-defined demographic population data for different regions of Australia to, for the first time, provide baseline estimates of incidence and prevalence that are relevant in the Australian setting. This will be the focus of the next part of this Ecosystem of Parkinson's Project.

7. Conclusions

A comprehensive assessment of extensive literature surrounding the incidence and prevalence of Parkinson's disease yielded no previous incidence estimates from Australia and seven previously published articles presenting primary data for prevalence in Australia. These estimates provide a huge range of possible prevalence values ranging from 66 to 850 per 100,000 with considerable uncertainty around all estimates.

International literature highlights the importance of considering population structure and diagnostic criteria in the estimation of incidence and prevalence. Two previous systematic reviews with meta-analyses provide solid age and sex stratified data for PD incidence and prevalence from previously published, high quality door-to-door surveys. These reviews suggest that considering a fine-grained population structure, based on age and sex distribution, and using these meta-analysed estimates, is likely to be the most robust method of estimating incidence and prevalence in Australia in lieu of additional high-quality local primary door-to-door survey data (Hirsch et al., 2016; Mellick, 2013; Pringsheim et al., 2014).

Given the lack of any extensive incidence and prevalence figures across different geographical regions in Australia, it is recommended that modelling of these figures be done using the available demographic data (from the Australian Bureau of Statistics) and the age and sex stratified estimates of incidence and prevalence generated from the available meta-analyses. Such estimates may provide the initial basis for understanding resource distribution and informing future studies to test the assumptions of these numbers or discrepancies that may result from the presence of risk factors or other previously unidentified determinants of disease presentation and outcome.

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**We thank you for your continued support
in our efforts to contribute to knowledge
about Parkinson's.**



Contact

Parkinson's Australia Ltd

Infoline 1800 644 189

www.parkinsons.org.au

info@parkinsons.org.au

[@parkinsonsaust](#)