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Hospitalisation and comorbidities in Parkinson's disease: A large Australian retrospect study

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HOSPITALISATION AND COMORBIDITIES IN PARKINSON'S DISEASE: A LARGE AUSTRALIAN RETROSPECTIVE STUDY

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RESEARCH DISSERTATION DECLARATION:

I, Michal Lubomski, principal researcher confirm that the content of this research thesis is my own work and contains no material which has been accepted for the award of any other degree or diploma in any university or other institution.

To the best of my knowledge, the thesis contains no material previously published or written by another person, except where acknowledged and appropriately cited.

Both supervisors, Professor Louise Rushworth and Dr Stephen Tisch, two co-authors of this project and publication have kindly provided their time in editing and clinical reasoning throughout the course of the Master's research project.

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1.0 CHAPTER 1 – INTRODUCTION TO MASTERS PROJECT

Project Title:

Hospitalisation and comorbidities in Parkinson's disease: a large Australian retrospective study.

1.1 Summary

Parkinson's disease (PD) is a progressive and disabling neurological disorder that affects approximately 1% of the adult population aged over 65 years in Australia. Parkinson's disease, as with many other chronic illnesses, results in frequent patient hospitalisations. There is a paucity of information on the causes and related co-morbidities that lead to hospitalisation among these patients in an Australian setting. The aim of this study was to examine patterns of hospitalisation of Parkinson's disease patients with regards to demographic factors, co-morbidities and aspects relating to clinical management. In this study, data was extracted from the NSW Ministry of Health's Admitted Patient Data Collection (APDC), to examine patterns of patient admission over a five-year period. A comparison group (patients without Parkinson's disease) was used to strengthen the study and to compare the epidemiological, demographic and clinical features of Parkinson's disease patients with those of patients without Parkinson's disease. Statistical analysis of patterns of disease that may predispose Parkinson's disease patients to hospitalisation was undertaken. The results of this retrospective study were used to inform patient groups and health care providers about possibilities for improved health outcomes for patients and their carers and were published in the Journal of Neurology, Neurosurgery and Psychiatry in 2014.

The first chapter of this Thesis introduces the research project, explaining the nature of the study with a brief description of the overall project. It further provides an overview of the remaining chapters and the layout of the research dissertation. The second chapter of this research dissertation provides an overview of the project's background, inclusive of an introduction to the study. It introduces the pathophysiology to Parkinson's disease, as well as evaluating its epidemiology in Australia, in addition to assessing different approaches to management. Learning experiences, challenges and major accomplishments are discussed in

Chapter 3. The results of the project are presented in Chapter 4 in the form in which they were published in the JNNP. A detailed overview of the study's methodology and statistical analysis is provided in Chapter 5. A critical appraisal and discussion of the study's significant findings as well as aspects of the design and analysis are discussed in Chapter 6. Chapter 7 comprises a conclusion section and a discussion on the knowledge and insights that I have acquired as a maturing researcher. It also includes a section on future directions and the evolution of my research interests.

Lastly, a detailed appendix section is included. This includes information regarding ethics approval documents. A copy of the cover letter to the Journal of Neurology, Neurosurgery and Psychiatry (JNNP) editor is also provided. Finally, a short reflection of this project's recent poster presentation at the Movement Disorder Society Australia (MDSA) Congress of Parkinson's Disease and Movement Disorders – 2014 – Queenstown (New Zealand), as well as its publication in Neurology Update is also included for reference.

2.0 CHAPTER 2 – BACKGROUND

2.01 Introduction

Parkinson's disease is a chronic, disabling and progressive neurological disorder of the basal ganglia within the central nervous system. This disease process results in a disruption of dopaminergic neurotransmission, leading to deregulated motor control, as a consequence of impaired feedback control mechanisms between various basal ganglia and the cerebral cortex. Histopathological examination demonstrates significant loss of dopaminergic neurons within the substantia nigra, with cytoplasmic inclusions (Lewy Body) deposition across cortical and subcortical structures. (1) This process leads to the ultimate development of extrapyramidal features, which are well recognised with Parkinson's disease. These include involuntary movements, a rest tremor, cogwheel rigidity, and slowness in movement (bradykinesia). Cognitive impairment may also develop at a later stage as the disease progresses. (2)

Idiopathic Parkinson's disease is the most prevalent form of the disease, affecting approximately 80% of all patients with Parkinsonian features. (3) The remaining patients manifest the parkinsonian phenotype as a consequence of a number of other causes. These include toxins, such as MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine), infections of the central nervous system, structural lesions of the brain including ischemia, metabolic disorders and exposure to neuroleptic medication. (1) Aside from secondary parkinsonism due to medications and ischemia, most of these causes are rare and are often able to be differentiated by history, examination and neuroimaging.

Advancing age is the most common risk factor for developing Parkinson's disease. However, there is an increasing body of evidence suggesting that genetic influences may have a role in the development of this disease, particularly if the age of onset is below 50 years. (4) Approximately 15% of people with Parkinson's disease have an affected first degree or second-degree relative. (4) Other epidemiological studies suggest that male gender is associated with an increased risk of developing Parkinson's disease, in addition to a an inverse relationship being observed with tobacco use and caffeine consumption. There are also indications that environmental factors (pesticide exposure), occupation, elevated blood

urate levels, NSAID use, and brain injury may also have a limited role in the development of this illness. (5)

Parkinson's disease is a complex illness that manifests in a number of cardinal motor signs and symptoms, which include rest tremor, rigidity, bradykinesia, and postural instability. Common non-motor symptoms include anosmia, constipation, Rapid Eye Movement (REM) sleep behaviour disorder, depression and cognitive impairment. (1, 6) The symptoms experienced by patients can vary according to the age of onset, disease duration and severity. The levels of disability and impairment can be profound, especially in the latter stages of disease. Patients often require increased care as the disease progresses due to increasing levels of disability, which impede the ability to manage daily tasks, such as bathing, dressing and meal preparation. (7) Depression is a common problem and this may reduce a patient's quality of life substantially. (8)

Standardised scores assist clinicians to assess aspects of the severity of the patient's disease and disability. Motor scores are frequently assessed by UPDRS scale (Unified Parkinson's Disease Rating Scale), with higher levels on this scale indicating more severe disease. (9) The Hoehn and Yahr Scale has been traditionally used to depict the stages of Parkinson's disease relating to impairment or disability: 0 to 1 – mild disease, 2-3 moderate impairment and 4-5 severe disability. (10)

Early diagnosis and treatment of Parkinson's disease can positively influence the patient's experience of living with the disease and that of their family and carers. (11, 12) Misdiagnosis and delayed presentation contribute substantially to patient anxiety and diminished perceptions of self-efficacy in managing the illness and this, in turn, can reduce the patient's quality of life. (12) In particular, older age, poor cognition and lower levels of mobility are determinants of sub-optimal outcomes for patients (13) Comorbidities also significantly influence the health outcomes of patients, particularly in the context of advancing age. (14) It has been shown that multiple medical system comorbidities occur frequently in people with mild to moderate Parkinson's disease and advanced age, with

recommendations suggesting that early intervention, particularly screening for balance and gait impairment, is important to delay the development of mobility disability. (15)

A further important predictor of health related outcomes for patients with Parkinson's disease is their access to a range of allied health services, which commonly include physiotherapy, occupational therapy, and speech therapy. In addition, some patients are benefited by psychological interventions, as well as the provision of social support services. (14, 16-18) However, it has been demonstrated that patients with a higher number of comorbidities and advanced age are the least likely to benefit from access to these support services. (17, 18)

2.02 Incidence And Prevalence

In Australia, there are approximately 8,900 new cases of Parkinson's disease each year and the illness is slightly more common in men than women. (19) The median life expectancy from disease onset to death is 12.2 years. (19) Due to the aging of the Australian population, the prevalence of people living with Parkinson's disease is expected to increase substantially over time and it is estimated that by 2025 there will be approximately 98,500 people living with Parkinson's disease, resulting in a greatly increased demand for health services. (19) Despite its prevalence, there is a paucity of information within Australia about the use of health services according to the age of the patient, or the duration or clinical severity of the illness.

Parkinson's disease is the second most common neurological disorder in Australia and approximately 30 Australians are diagnosed with Parkinson's disease every day. Parkinson's disease affects patients in all age groups but is more common among older people, with a peak incidence in the early 60-year age group. It has an estimated prevalence of one percent after the age of 65 years. (20) However, Parkinson's disease can also affect younger people, (typically less 50 years of age), with 20% of those affected being of working age. (21) This often places increased financial and social strains on younger families, which often include children. The incidence of Parkinson's disease can vary between populations, with the highest prevalence being found in Caucasian populations. (22) In addition, there is some

evidence to suggest that Parkinson's disease is more common in rural than metropolitan areas in Australia. (23)

2.03 Clinical Management

Although medical treatment with dopamine replacement is the primary management option for most patients with this disease, a variety of surgical and rehabilitation options have been shown to be of additional benefit. (24) Common surgical interventions for patients with predominantly motor fluctuations include Deep Brain Stimulation or various lesioning techniques, which are less commonly utilised in modern practice. (25) Rehabilitation goals can vary between patients, however therapy typically focuses on gait and balance, postural stability, as well as falls prevention. (26) Higher levels of impairment and increased restrictions due to progressive disease result in many Parkinson's disease patients being referred to allied health services. These include speech therapy for swallowing and aspiration assessments; occupational therapy to assist with functional independence, including provisions of walking aids and modifiable home installations; and physical therapy to improve muscle strength and balance with the aim of minimising falls. (26) In addition, there is evidence to suggest that a multidisciplinary approach between the various health care providers can optimise health outcomes for patients. (16) However, for many patients, access to such services can be sporadic and uncoordinated, particularly across regional and remote areas. (27) Furthermore, access to health services, including allied health and psychological support services can vary between population sub-groups depending on their income and ability to afford private health insurance. (28, 29)

Patient comorbidities have a significant impact on the clinical management of Parkinson's disease patients, both in the inpatient and outpatient setting. This is particularly evident in relation to the effects of polypharmacy to treat a variety of comorbidities that may, in turn, result in the deterioration of another condition, thus leading to more complicated management and a potential risk for subsequent hospitalisation. Common adverse drug reactions include: worsening of motor symptom control secondary to neuroleptic medications that are used in behavioural and hallucination management; postural hypotension secondary

to antihypertensives; and worsening bowel and bladder control, delirium and cardiac arrhythmias that may occur with advancing Parkinson's disease and Levodopa use in combination with cholinesterase inhibitors that are used for the management of cognitive impairment. It is often necessary to adjust Parkinson's disease patient medications in response to changes in the clinical situation, as well as to address interactions that may occur in relation to coexisting medical problems. (30-32)

2.04 Hospital Management Of Parkinson's Disease

Hospital services play an important role in the management of Parkinson's disease, especially when the symptoms of the disease are particularly intrusive. In Australia, in 2009-10, there were 3179 hospitalisations for Parkinson's disease as a primary diagnosis nationally. (21) However, this is likely to be an underestimate, especially in relation to the identification of Parkinson's disease as a secondary diagnosis, which may either remain undiagnosed or may not be recorded in the discharge summary.

Hospital admission may be a reflection of inadequate outpatient care, either due to an inability to access necessary services or due to compliance issues. Admission to hospital is also infrequently used to clarify a Parkinson's disease diagnosis, using a levodopa challenge. Hospitalisation for Parkinson's disease patients carries significant risks of complications, which may be related to, for example, adverse drug reactions, delirium and falls. These may be attributable to existing comorbidities or natural disease progression. Despite this, there is a paucity of information on the underlying reasons for admission to hospital among Australian patients with Parkinson's disease. In addition, there is very little information on the distribution of co-morbidities of Parkinson's disease patients who are admitted to hospital. (7, 19)

Although motor disturbances in Parkinson's disease are believed to be a significant cause of Parkinson's disease related admissions, other less defined causes are likely to influence hospitalisation, particularly non-motor complaints. Nationally it was estimated that in 2009-10, 2220 hospital admissions were recorded for accidental falls as well as 2138 admissions

for pneumonia in the context of Parkinson's disease related complications. (21) This was predicted to cost at least an additional $76.6 million to the health system. (21) Further, information regarding the types of health services used by hospitalised Parkinson's disease patients during their hospital stay is largely unavailable in an Australian hospital setting. (33)

Although it is recognized that Parkinson's disease patients are admitted to hospital at higher rates than other groups and frequently have longer stays than the general population, (30) few formalised interventions have been implemented with the aim of reducing the need for hospitalisation or for minimising the incidence of inpatient related complications. (30, 34, 35) A systematic review of the limited global literature investigating the reasons for admission and the impacts of Parkinson's disease complications during an inpatient stay, identified higher incidences of aspiration pneumonia, trauma (inclusive of fractures), psychosis and sepsis in Parkinson's disease patients than among controls. (30) In addition, a recent systematic review from the Netherlands suggested that Parkinson's disease patients have a hospital stay of between 2-14 days longer than controls, with 7 to 28% of Parkinson's disease patients being admitted to hospital each year. (36)

2.05 Reasons For Admission

Admissions to hospital for patients with Parkinson's disease may either be planned or due to an acute problem needing immediate hospital management. In Parkinson's disease, the diagnosis may be the principal cause of admission (the disease that contributed most to the length of stay) or, alternatively, Parkinson's disease may be a comorbidity that makes the management of the patient's principal problem more complicated. Accordingly our study was designed to investigate differing types of admissions for Parkinson's disease, either as a principal or a secondary diagnosis. This enabled the investigation of the patterns of comorbidities in hospitalised patients with Parkinson's disease.

In one Australian study conducted in 2006, patients with a primary diagnosis of Parkinson's disease presented with the following problems as reasons for admission: falls and fractures

(13%), pneumonia (12%), cardiac issues/syncope (16%) and gastrointestinal disorders (11%). (33) A systematic review (30) of the four major worldwide studies investigating reasons for admission in patients with a diagnosis of Parkinson's disease, identified motor complications, falls and fractures, as well as pneumonia, as being the most common factors that precipitated the need for hospitalisation. (33, 35, 37, 38) Fluctuating motor control is a known significant predictor of hospitalisation, with complications arising from the motor impairment being a causal factor for higher rates of inpatient admissions, (30) with approximately 15% of admissions requiring active management for the primary motor syndrome. (33)

Many challenging clinical features are encountered in managing the hospitalised Parkinsonian patient. Early recognition and management of these possible problems may optimise the potential benefits of an inpatient stay, along with decreasing hospitalisation-related complications. An overview of some of the important considerations that influence clinical decisions during hospitalisation of a Parkinson's disease patient is given below.

2.06 General Principles

There are a number of general principles that guide the management of patients with Parkinson's disease in hospital. First, an early and complete assessment of medications, dosages and specific dose schedules is regarded as being the key step in minimising medication errors in hospital, as many of the medications are time critical. (30) Further, in order to prevent serious sequelae, it is vital to give consideration to the life threatening, although rare, risk of Neuroleptic Malignant Syndrome (NMS) that can arise with the sudden discontinuation of medications. (31) Formal assessment of mobility with physiotherapy is encouraged, particularly for the assessment of falls risk and rehabilitation requirements. Guidelines currently under development encourage formal evaluation of swallowing by speech therapists, as the risk of aspiration is often underestimated. (39)

2.07 Infections

Patients with Parkinson's disease are at a significant risk of developing aspiration pneumonia, as a result of difficulties with swallowing. A Chinese study has shown this to be the most commonly reported cause of inpatient death in Parkinson's disease. (40) Measures including teaching chin down swallowing and the introduction of nasogastric feeding have been successfully employed to prevent aspiration pneumonia. Furthermore, infections secondary to reduced mobility such as cystitis and decubitus ulcers have been shown to precipitate delirium in Parkinson's disease, thus early aggressive antibiotic treatment has been shown to decrease rates of encephalopathic complications in the context of hospitalisation and ambulatory care. (40-42)

2.08 Delirium

There are a myriad of potential factors that can predispose an inpatient with Parkinson's disease to an increased risk of delirium. These include: an unfamiliar environment; infection; changes in medications; the effects of drugs and anaesthesia; and constipation and pain. (30) Commonly prescribed medications that are centrally active pose the highest risk of encephalopathy. These include pharmaceutical agents from the classes of: benzodiazapines, other anxiolytics, narcotics, hypnotics and antidepressants. Other drug related delirium effects may result from the use of anticholinergic drugs, some antiemetics and some antihypertensive medications. Pharmacological treatment of delirium in Parkinson's disease necessitates the avoidance of typical neurolepitcs due to their propensity to exacerbate motor dysfunction, including rigidity. International guidelines now stipulate the use of atypical neuroleptics such as quetiapine or clozapine, in the context of delirium or psychosis in Parkinson's disease, as these have not been shown to cause motor dysfunction. (30, 35, 43)

2.09 Falls And Fractures

Falls and fractures are one of the most common reasons for hospital admission in patients with Parkinson's disease, with estimates of their occurrence ranging between 13-24% of all

hospital admissions. (33, 35, 37) Hip fractures are known to occur commonly in the context of Parkinson's disease. (44) Pneumonia and delirium are known precipitants of admissions for fractures, as well as being commonly encountered complications post operatively. (30) Unfortunately no guidelines have been published that direct the management of patients who suffer from hip fractures. Generally the approach is to institute measures that are aimed at falls prevention; treatment of low bone density, including bisphosphonates and Vitamin D; and the provision of physical assistance devices, including ambulatory aids, such as canes, walkers and wheelchairs. (30)

2.10 Hypotension / Syncope

Orthostatic hypotension, which is a common cause of syncope in patients with Parkinson's disease, is mediated by disease related autonomic instability as well as by the effects of medication, particularly levodopa. (30) Indeed, it has been found that syncope is one of the leading causes of hospitalisation in Parkinson's disease patients, occurring in approximately 11% of those requiring hospitalisation. (30) Measures aimed at correcting hypotension focus on reductions in anti-hypertensive medications, and ensuring appropriate fluid intake, with a possible increase in salt consumption. Further pharmacological measures include the addition of the mineralcorticoid, fludrocortisone, as well as arterial pro-contraction agents such as midodrine. (30)

2.11 Venous Thrombosis

Venous thromboembolism (VTE) is a serious complication that can arise in Parkinson's disease, even during short hospital admissions. In Parkinson's disease, pulmonary embolism has been identified as being the second most common cause of inpatient death. (45) Appropriate prophylactic anticoagulation for VTE along with mechanical measures have been recommended to prevent VTE related inpatient complications.

2.12 Psychiatric Issues

Aside from the inpatient treatment for psychosis or delirium, as previously discussed, depression and anxiety are common psychiatric syndromes that require careful supportive management, often by pharmacological means. Treatment of depression with low dose tricyclic antidepressants (TCAs), as well as selective serotonin reuptake inhibitors (SSRIs), have been shown to significantly improve outcomes while offering minimal adverse effects. (46, 47) Refractory or medication resistant depression has been successfully treated with electroconvulsive therapy (ECT), where additional benefits in motor improvement lasting several weeks have also been observed. (47-49) Anxiety in Parkinson's disease frequently presents with shortness of breath (30) or with concern about the medication "wearing off" phenomenon. (50) Benzodiazepines have been suggested as effective treatments for anxiety in this situation, however these medications predispose patients to an increased risk of falls, somnolence and confusion. Thus their use in anxiety should be carefully considered.

2.13 Elective Hospitalisation And Parkinson's Disease

There is wide international variation in the reported numbers of elective admissions for patients with Parkinson's disease. (51) A recent Italian study suggested that as many as 20% of Parkinson's disease hospitalisations were planned. Commonly occurring planned admissions included musculoskeletal ailments, rehabilitation and cardiovascular disease management (52) In other studies, the reasons for elective admission included: elective surgery, rehabilitation, and medication management including drug holidays. (30) Tertiary centres report Deep Brain Stimulation (DBS) as the most common cause of elective hospitalisation in Parkinson's disease. (30) Reports of elective surgery in patients with Parkinson's disease have identified longer hospital stays, higher in-hospital mortality, as well as increased post-operative complication rates compared to controls. (34) However, early neurologic consultations for elective orthopaedic surgery have been shown to result in improved surgical outcomes and a reduced length of stay. (53)

2.14 Elective Surgery

Elective surgery predisposes a patient with Parkinson's disease to an increased risk of delirium. Appropriate education and discussion of this risk with the patient and family may reduce the need for unnecessary post-operative investigations for causes of delirium should this occur. (30) Daily review and rational balancing between adequate analgesia and delirium risk has been recommended as good practice for Parkinson's disease surgical patients. (30) Post operative complications due to gastric stasis pose challenges to ongoing medication administration, as there are no approved parenteral formulations for use in Parkinson's disease. Recently however a dopamine agonist transdermal patch (Rotigotine) has been shown to be beneficial in the perioperative setting for management of Parkinson's disease patients who are unable to receive oral medication. (54) Gastric stasis can result in an acute dopamine medication discontinuation, predisposing patients to the rare but serious effect of Neuroleptic Malignant Syndrome. (30) Suggested measures to avoid disruptions with time critical medication administration in Parkinson's disease may include the alternative use of a dopamine agonist patch (Rotigotine), apomorphine subcutaneous infusions or the temporary insertion of a nasogastric tube for medication administration. (30)

2.15 Keeping Parkinson's Disease Patients Out Of Hospital

Improved access to urgent outpatient Neurology Clinics has been shown to significantly reduce inpatient Parkinson's disease hospitalisations according to a recent Israeli study. (35) This study identified that keeping an 'open door policy' to urgent outpatient Neurology Clinics was a successful means of reducing 50% of yearly admissions, as well as reducing the overall length of stay by 4 days. (35) Further, outpatient liaison, with ongoing input from speech therapy, occupational therapy, physiotherapy as well as neuropsychology, has also been shown to decrease the need for hospitalisation. (30)

2.16 Causes Of Death In Parkinson's Disease

A recent review of deaths due to Parkinson's disease in Australia showed that in 2011, 1692 people died due to the disease with very little information available about the exact causes of death. (21) With the predicted aging of the Australian population over the coming decades, these projections are expected to rise sharply, placing extra strain on hospitals, nursing homes, and the community to provide supportive services for people with late stage Parkinson's disease. (21) Early international studies have identified that respiratory infections were the most common cause of out and inpatient Parkinson's disease deaths. (55) Autonomic dysregulation was suggested as a potential causative mechanism in these deaths. (55) More recently, in a British study, pneumonia was documented as the terminal event in 45% of the deceased Parkinson's disease patients. (56) In another review of common causes of death documented in death certificates identified: malignancy, ischemic heart disease, cerebrovasuclar disease, chronic lung disease, heart failure and dementia. (57) Interestingly death from malignancy and ischemic heart disease was lower in Parkinson's disease patients than in controls. (56) However significant limitations in the documentation of the cause of death were commonly identified, with estimates of inadequate information in approximately one third of death certificates. (56)

A Canadian analysis identified that pulmonary embolism was the second most common cause of death, after respiratory infections, on autopsy examinations. (45) These authors suggested that other estimates of the causes of Parkinson's disease deaths may have been misleading due to a lack of pathological / autopsy information. (45) Overall, estimates suggest that persons with Parkinson's disease are at a 43% greater risk of all-cause mortality. Importantly, these patients have a 51% greater risk of injury-related mortality compared with the general population. (58) There is, however, a paucity of information about the causes of inpatient Parkinson's disease deaths in Australia.

2.2 Discussion

The literature review presented in the preceding paragraphs describes the current knowledge of the role of hospitalisation in the management of Parkinson's disease; the best measures to optimise care of these patients; and the impact of comorbidities on patient outcomes. However, knowledge about the reasons underlying admission among patients with either a principal or secondary diagnosis of Parkinson's disease, as well as the effect of comorbidities on hospitalisation in Parkinson's disease is incomplete.

This research project aims to address this deficiency in the international literature. First, it aims to describe the associations between demographic characteristics and comorbidities of Parkinson's disease patients who have received hospital care and important health-related outcomes. Second, it aims to provide some information on service delivery to patients, including variations in access to advanced Parkinson's disease therapies, including DBS. This research will add to the international literature by providing a large state-wide population analysis of Parkinson's disease hospitalisations. By doing this, it is hoped that it will inform the tailoring of better service provision to patients with Parkinson's disease.

3.0 CHAPTER 3 – DEVELOPMENT OF THE RESEARCH PROJECT

3.1 Introduction

This research project was devised in response to the neuro-epidemiological research into Parkinson's disease that was part of my Medical Research Honours Project at The University of Notre Dame, Australia in 2011. This prompted the development of a larger scale study investigating the health related issues associated with Parkinson's disease hospitalisation. Given the increasing prevalence of Parkinson's disease within Australia that is due to the ageing of the population, it was of concern that there was not a well-developed understanding of the reasons for hospitalisation in Parkinson's disease in Australia, nor about the comorbidities that are associated with admission.

My experience of clinical practice within the Neurology Department at St Vincent's Hospital in Sydney, as an Intern and later as a Basic Physician Trainee, provided further exposure to patients with Parkinson's disease and gave me insight into the complexities of managing hospitalised patients with Parkinson's disease. This exposure led me to develop a greater research interest into improving the characterisation of the nature of Parkinson's disease patient hospitalisations, investigating differences in patients admitted purely for management of their Parkinson's disease compared with those admitted with Parkinson's disease as a comorbidity, in general, and with regards to patient outcomes.

A working relationship was fostered in early 2013 between myself, Dr Stephen Tisch, consultant neurologist and staff specialist, who co-ordinates the Movement Disorder clinic at St Vincent's Hospital, and Associate Professor Louise Rushworth, medical epidemiologist from The University of Notre Dame. Together we developed a strategy to undertake a comprehensive analysis of hospitalised patients with Parkinson's disease in NSW. A literature review investigating the determinants and demographics of Parkinson's disease in Australia was completed. This highlighted the problem of a paucity of local and national knowledge in this area. This, in turn, informed the objectives of our study. Subsequently, negotiations began with the NSW Ministry of Health to formulate appropriate inclusion and

exclusion criteria for the extraction of a study sample and comparison group from the State data collection on hospital admissions.

Ethical approval from Human Research and Ethics Committees from the University of Notre Dame was obtained prior to undertaking the study. This required the completion of a low-risk application form because the data was non-identifiable and had already been collated for funding and resource allocation purposes by the NSW Ministry of Health. The Ethics Application Form to the University of Notre Dame in detail is attached in Appendix 1.

3.2 Aims And Objectives

This project had three aims. They were:

1. To examine Parkinson's disease patient hospitalisations in New South Wales over a 5 year period and to describe the patient demographics, reasons for admission (for both principal and secondary diagnoses), aspects relating to clinical management and services accessed during an inpatient admission and to compare these patient characteristics with a sample of patients admitted to NSW hospitals without a diagnosis of Parkinson's disease, weighted according to the age and sex distribution of Parkinson's disease patients in the general population.
2. To examine associations between co-morbidities and clinical aspects of Parkinson's disease management.
3. To estimate the frequency of inpatient mortality in hospitalised Parkinson's disease patients.

3.3 Hypothesis

1. Patients with Parkinson's disease present with problems related to their chronic neurological illness that are likely to directly influence their health outcomes during hospitalisation.
2. Demographics, co-morbidities and clinical management are likely to differ between Parkinson's disease patients and a comparison group.
3. Patients with higher numbers of co-morbidities relating to their diagnosis of Parkinson's disease are likely to have a prolonged and complicated admission, possibly with a higher incidence of in-hospital mortality than control patients.
4. Co-morbidities not related to Parkinson's disease are likely to result in complicated inpatient management and increase the patient's length of stay and may be reflected in higher rates of in-hospital mortality than control patients.

3.4 Learning Experiences and Challenges

During the course of the research project many new learning experiences and challenges arose which shaped and directed the project. The development of the research focus continued on from experiences that I had had through my Honours research, investigating regional and urban differences in the Quality of Life (QoL), clinical management as well as allied health utilisation of Parkinson's disease patients. A subsequent publication focusing on clinically important differences between the genders in the same cohort provided a greater in-depth understanding of outpatient clinical management of Parkinson's disease.

The Master's research focus was thus directed at studying the effects of inpatient management to provide a more comprehensive understanding of the complexity of medical care involved with the management of Parkinson's disease. Particular focus on the investigation of the causes of hospitalisation, in addition to the distribution of comorbidities of Parkinson's disease patient presentations, was performed. A literature review evaluating a variety of clinical inpatient management implications for Parkinson's disease gave rise to a presentation

at the University's Research Symposium in 2013, focusing on strategies to improve Parkinson's disease inpatient care.

Further learning experiences included close collaboration with the NSW Ministry of Health to develop acceptable criteria for data extraction. Mr John Agland, manager of Performance Reporting Health System Information and Performance Reporting Branch NSW Ministry of Health was instrumental in fostering a close working relationship with his analyst, Mr Jithendra Uppalapati to facilitate data extraction. The Ministry of Health did not undertake any data analysis or selection of subsamples for analysis, with only raw tabulated data being provided for the project, (see Chapter 5 – Methods). The handling of this vast dataset proved to be quite a challenging task, as multiple databases had to be generated and integrated to provide a dataset on all public and private Parkinson's disease hospitalisations over the 5 year study period. Data acquisition could only be obtained after completion and clearance from the University's Human Research and Ethics Committee.

Several of the most significant challenges of this project included the functional integration and analysis of thousands of individual data points in Excel and SPSS. With an initial database comprising more than 14,000 patient admissions, prior to applying exclusion and inclusion criteria, significant database construction and programming were required. However the most challenging aspect of the project was the transformation and collation of the vastly differing diagnostic and procedural codes that required clustering into workable categories. This analytical work required the input of a senior analyst, Mihovil Matic. Subsequently, varying ICD-10 codes (59) were later recoded into clinically appropriate domains relating to Parkinson's disease, as referred to in the journal publication – Tables 3 and 4.

Significant consideration was given to selecting a representative sample of Parkinson's disease patients. Difficulties arose when applying exclusions to different types of admissions including those to an inpatient psychiatric, rehabilitation or dialysis ward, as the study was focused on admissions for general issues in this patient group. The same exclusions were applied to the comparison group. After these exclusions, it was found that there were more short stay admissions, for a variety of day procedures in the comparison sample. A critical

analysis of the study groups and the design of the project are further explained in Chapter 6 – Discussion.

Finally, the definition and extraction of an appropriate comparison group was another technical challenge. There were many difficulties in preparing this dataset due to the separation of the NSW Ministry of Health's public hospital and private hospital databases. As multiple inclusion/exclusion criteria needed to be applied, only one year's (2008) admissions were extracted to constitute the comparison group for the analysis. This, however, provided a sufficiently robust comparison group with which to compare the Parkinson's disease population. The structure of the comparison group has also been described in the journal article, which forms Chapter 4 of this thesis.

3.5 Major Accomplishments

The greatest accomplishment of the research project was its ability to report on an analysis of a large number of Parkinson's disease admissions throughout NSW over a 5-year timeframe. This type of study has not been done in Australia for Parkinson's disease patients before now.

The most significant results of the project relate to the newly identified differences that were found between Parkinson's disease patients and the comparison group with regards to the reasons for hospitalisation. The results demonstrated that Parkinson's disease patients were five times more likely to be treated for delirium, three times more likely to experience an adverse drug event and syncope, more than twice as likely to require management of falls/fractures, dementia, gastrointestinal complications, genitourinary infections, reduced mobility and other trauma but half as likely to require hospitalisation for chronic airways disease and neoplasia, including melanoma, compared to patients without Parkinson's disease.

Further, another notable accomplishment achieved during the project was the acceptance and presentation of a poster at the 2014 Movement Disorder Society of Australia conference in Queenstown, New Zealand. This received the 1st prize for the poster presentations, which was a great honour. Further, an abstract was also accepted in the International Movement Disorder Congress in Stockholm, 2014. Importantly, it also fostered a further interest in pursuing a career in Neurology, preparing me for subsequent clinically directed research, which I hope to continue throughout Neurology Advanced Training. Lastly, the successful publication of the study within the Journal of Neurology, Neurosurgery and Psychiatry (JNNP) with an impact factor: 4.924, was a highly rewarding accomplishment for all the researchers involved.

As per the journal's disclosure: *The JNNP's ambition is to publish the most ground-breaking and cutting-edge research from around the world. Encompassing the entire genre of neurological sciences, our focus is on the common disorders (stroke, multiple sclerosis, Parkinson's disease, epilepsy, peripheral neuropathy, subarachnoid haemorrhage and neuropsychiatry), but with a keen interest in the Gordian knots that present themselves in the field, such as ALS. With early online publication, regular podcasts and an immense archive collection (with the longest half-life of any journal in clinical neuroscience), JNNP is a trail-blazer and not a follower.*

4.0 CHAPTER 4 – RESEARCH MANUSCRIPT / PUBLICATION

Publication in the Journal of Neurology, Neurosurgery and Psychiatry: June - 2014

Email verification of the article's publication has been sent to Prof George Mendz (Head of Research), University of Notre Dame, Sydney School of Medicine.

RESEARCH PAPER

Hospitalisation and comorbidities in Parkinson's disease: a large Australian retrospective study

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ABSTRACT

Objectives Patients with Parkinson's disease (PD) require higher levels of care during hospitalisation. Management of comorbidities in these patients aims to optimise function while minimising complications. The objective of this study was to examine patterns of hospitalisation of patients with PD in NSW with regards to sociodemographic factors, comorbidities and aspects of clinical management.

Methods A retrospective study of all patients with idiopathic PD and a control group of non-PD patients admitted for acute care to NSW hospitals between 2008 and 2012.

Results The study group comprised 5637 cases and 8143 controls. The mean PD patient age was 75.0 years (±10.9). Patients with PD had a significantly longer hospital stay (median 7 days, IQR 3–13 vs 1 day, IQR 1–7, p<0.001) than control patients. Patients with PD were five times more likely to be treated for delirium, three times more likely to experience an adverse drug event and syncope, more than twice as likely to require management of falls/fractures, dementia, gastrointestinal complications, genitourinary infections, reduced mobility and other trauma but half as likely to require hospitalisation for chronic airways disease and neoplasia, including melanoma, than the control group (all p<0.001).

Conclusions Patients with PD are more likely to suffer serious health problems, including delirium, adverse drug reactions, syncope, falls and fractures than controls. These findings highlight PD as a multisystem neuropsychiatric disorder in which motor and non-motor features contribute to morbidity. Increased awareness of the added risk PD poses in acute hospitalised patients can be used to inform strategies to improve patient outcomes.

INTRODUCTION

Parkinson's disease (PD), which affects approximately 3.4% of adults over 55 years,[1] is a common progressive and disabling neurological disorder characterised by the degeneration of several different neuronal populations important for movement, autonomic function and cognition. There is a worldwide paucity of information on the causes and related comorbidities that lead to hospitalisation in patients with PD.[2] Rising life expectancy is increasing the prevalence of chronic diseases such as PD, and it is estimated that there will be between 8.7 and 9.3 million people over the age of 50 years living with PD around the world by 2030.[3] In Australia, the incidence of PD is approximately 8900 cases per year, and it is slightly more common in men than women.[4–6] In 2009–2010, there were 3179 patients treated in hospital for PD in Australia.[7]

Many challenging clinical features and comorbidities are encountered in managing the hospitalised patient with PD. Early recognition and management of these issues aims to optimise the potential benefits of an inpatient stay, along with decreasing hospitalisation-related complications.[8 9] Although complications including falls, fractures and reduced mobility are believed to be a significant cause of PD-related admissions, medical comorbidities including pneumonia, cardiac diseases and non-motor PD symptoms including cognitive impairment, psychiatric complaints and adverse drug events are likely to result in an increasing need for hospitalisation in patients with PD.[2 8–14] In Australia in 2009–2010, there were an estimated 2220 hospital admissions for accidental falls and 2138 admissions for pneumonia in the context of PD-related complications.[7]

Patients with PD are admitted to hospitals at higher rates and frequently have longer stays than the general population.[9 11 12 15] Admission for aspiration pneumonia, trauma (inclusive of fractures), psychosis and sepsis are higher in patients with PD than controls.[9] Further, patients with PD, on average, have a longer length of stay (LOS) of between 2 and 14 days than controls, with 7–28% of patients with PD requiring yearly hospitalisation.[16] Encouraging evidence supports improving access to outpatient clinics as an essential strategy to minimising inpatient hospitalisations.[11] The objective of this study was to examine patterns of acute care hospitalisation of patients with PD in NSW with regards to sociodemographic factors, comorbidities and aspects relating to clinical management.

METHODS

Study settings and subjects

The NSW Ministry of Health maintains a database, the Admitted Patient Data Collection (APDC) on all separations (episodes of hospitalisation) from public and private hospitals in NSW. Information stored in the APDC includes patient age, gender, principal diagnosis and all secondary diagnoses, any surgical procedures, hospital type, mode of admission (eg, through the emergency department or planned admissions) and separation (eg, discharge home, death, transfer to another hospital) and LOS.

For the purposes of this analysis, all patients with either a principal diagnosis or a secondary

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(comorbid) diagnosis recorded as Idiopathic Parkinson's disease (ICD-10-CM G20) and who had a separation (episode of care) from a NSW hospital (public or private) between the years 2008 and 2012 were included in the study. Exclusions included other causes of Parkinsonism: secondary Parkinson's disease, atypical Parkinson's disease, vascular Parkinsonism or Parkinson's Plus Syndromes. Admissions for inpatient rehabilitation, dialysis or to an inpatient psychiatric facility were excluded from this analysis. Ethics approval was received from the University of Notre Dame Australia Human Research Ethics Committee.

Control group

A random sample of patients admitted to NSW hospitals during 2008 without a principal or secondary diagnosis of PD was selected as the control group for this study. As public and private hospital data are stored separately, the selection of the control group was first weighted according to the relative proportion of beds available in these two sectors in NSW (74% and 26%, respectively).[17] The control subjects were then selected using weights based on the age and gender distribution of the most recent Australian PD prevalence estimates, corresponding to a ratio of 1.10 males to 1 female and an age distribution of 6% (<55 year olds), 12% (55–64 year olds), 29% (64–74 year olds), 33% (75–84 year olds) and 20% (>85 year olds).[7] Patients were excluded from the control group if they were admitted for rehabilitation, dialysis or to an inpatient psychiatric facility.

Statistical analysis

All admission diagnoses were grouped according to the ICD-10 Chapter headings. (International Classification of Diseases, Tenth Revision).[18] Within these categories, diagnoses were grouped according to the clinical conditions related to PD. Cardiac diseases included myocardial infarction (I21) and conduction disorders (I44). Orthostatic hypotension (I95) and syncope and collapse (R55) were classified individually due to their specific relevance to PD. DBS insertion was represented by procedure codes: 92036 (insertion of intracranial electrode via burr holes) and 39138 (insertion of intracranial electrode via craniotomy).

Two-sample, independent t tests were used to analyse differences between the groups for continuous variables. As LOS was highly skewed, a Mann–Whitney U test was used to compare this variable between the groups. χ^2 tests were used to compare differences between categorical variables. Logistic regression models were constructed to evaluate differences in the prevalence of various health problems between the total PD and control groups after controlling for age, gender, marital status, hospital type and LOS. A 5% level of significance was used. Data analysis was performed using SPSS for Windows, V.20 (SPSS Inc, Chicago, Illinois, USA).

RESULTS

Demographic characteristics

There were 5637 patients receiving inpatient care for PD over the 5-year study period and these patients comprised the study subjects. These episodes of care for patients with PD represented approximately 0.04% of all the separations from NSW hospitals over that time and corresponded to a rate of 1127 separations/year from an estimated NSW PD patient population of 20 597 patients (54.7/1000 patients with PD per year).[7 19] Of these, 1574 (27.9%) separations were for PD as a principal diagnosis and 4063 (72.1%) as a secondary diagnosis. The control group consisted of 8143 patients who received treatment in a NSW hospital and who did not have either a principal or secondary diagnosis of PD. The demographic and hospitalisation characteristics of the study and control groups are shown in table 1.

The mean age of all patients with PD was 75.0 years (±10.9) (range 30–100 years), which was slightly higher than that of the control group (73.1 years (±13.9)). There were proportionally more men in the PD than the control group (62.8% and 52.9%, respectively, χ^2=131.4, df=1, p<0.001, table 1) and marital status differed significantly between the two groups (χ^2=235.0, df=3, p<0.001) with the PD group having a greater proportion of married or de facto couples than the control sample (62.8% vs 50.6%, respectively). Three quarters of the PD group were treated in a private hospital compared with only 30% of the control group (75.7% vs 30.3%, χ^2=2752.1, df=1, p<0.001).

Within the total PD patient sample, patients with PD as a principal diagnosis were younger (68.2±11.1 years vs 77.6 ±9.5 years, t=−31.7, df=5635, p<0.001, table 2); were more likely to be married or in a de facto relationship (73.6% vs 58.6%, χ^2=205.5, df=3, p<0.001) and be admitted to a private hospital (90.4% vs 70.1%, χ^2=253.7, df=1, p<0.001) than those with PD as a secondary diagnosis.

Clinical characteristics

Patients with PD had a significantly longer LOS than the control group (median LOS 7 vs 1 day, U test=13 705 361.0, df=1, p<0.001, table 1). There were also differences between the two groups with respect to the mode of admission (χ^2=199.4, df=2, p<0.001) with more patients with PD having a planned admission than controls (58.4% vs 51.3%). In addition, there were significant differences between the two groups in their mode of separation (discharge outcome) (χ^2=141.3, df=3, p<0.001). Fewer patients with PD than controls were discharged to their usual place of residence (69.4% vs 76.3%), and more patients with PD were transferred to other hospitals (13.5% vs 10.3%) or to nursing homes (5.8% vs 4.4%). There were 209 deaths in the total PD group, corresponding to an in-hospital mortality rate of 37.1/1000 separations, which was not significantly different from that in the control group (309 deaths or 38.0/1000, χ^2=0.1, df=1, p=0.722).

Within the sample of all patients with PD, those with a secondary diagnosis of PD had a longer LOS (median LOS 7 vs 6 days, U test=3 411 066.0, df=1, p<0.001, table 2). Differences were noted with respect to the mode of admission (χ^2=528.9, df=2, p<0.001) with more patients with a secondary diagnosis of PD being admitted through the emergency department than those with a principal diagnosis of PD (42.2% vs 12.0%). Further, there were significant differences between the two PD groups in their mode of separation (χ^2=215.5, df=3, p<0.001). Fewer patients with a secondary diagnosis than a principal diagnosis of PD were discharged to their usual place of residence (63.9% vs 83.7%); however, they were more likely to be transferred to other hospitals (16.2% vs 6.4%) or to nursing homes (6.7% vs 3.5%). There were 182 deaths in the group with a secondary diagnosis of PD, corresponding to an in-hospital mortality rate of 44.7/1000 separations, which was significantly higher than for those with a principal diagnosis of PD (27 deaths or 17.2/1000, χ^2=25.5, df=1, p<0.001).

Health problems during admission

The frequencies of a number of health problems recorded for patients with PD and the control group are shown in table 3. Among the patients with PD, the most common health

Table 1 Clinical and demographic characteristics during acute care admission of PD and control patients, NSW 2008–2012

	Total Parkinson's patients	Control	Test statistic	p Value
Number of patients (n=)	5637	8143		
Age (years) [SD]	75.0* [10.9]	73.1† [13.9]	t=8.6 (13 778)‡	<0.001
Gender (%)			χ^2=131.4 (1)§	<0.001
Male	62.8	52.9		
Female	37.2	47.1		
Marital status (%)			χ^2=235.0 (3)§	<0.001
Married/de facto	62.8	50.6		
Widowed	18.9	22.4		
Single	10.0	14.1		
Other	8.3	12.9		
Hospital type (%)			χ^2=2752.1 (1)§	<0.001
Public	24.3	69.7		
Private	75.7	30.3		
Average length of stay (days)			U test=13 705 361.0 (1)¶	<0.001
Median	7	1		
Interquartile ranges	3–13	1–7		
>20 days (%)	12.3	9.2		
Means of admission (%)			χ^2=199.4 (2)§	<0.001
Emergency	33.8	35.1		
Non-emergency/planned	58.4	51.3		
Other	7.8	13.6		
Mode of separation (%)			χ^2=141.3 (3)§	<0.001
Discharge by hospital	69.4	76.3		
Transfer to other hospital	13.5	10.3		
Transfer to nursing home	5.8	4.4		
Death	3.7	3.8		

*Range (30–100 years).
†Range (1–104 years).
‡(Independent sample t test).
§(Pearson's χ^2 test).
¶(Mann–Whitney U test) df (degrees of freedom).
PD, Parkinson's disease.
Bold text signifies statistical significant results.

problems were falls/fractures (19.8%); cardiac diseases (ischemic heart disease/heart failure/arrhythmia) (16.7%); complications arising from dementia (14.4%); deep brain stimulation management (DBS) (14.1%) and psychiatric illness (13.6%). There were 794 admissions for DBS, corresponding to a rate of 28.2/1000 patients with PD per year. Of these, (50.6%) were for insertion and management of the device, (15.6%) were for removal, while remaining admissions (33.8%) were for programming and management. Patients who had in-hospital DBS management were significantly younger (t=30.4, df=5636, p<0.001), were more frequently in a married or in a de facto relationship (χ^2=246.5, df=3, p<0.001) and were much more likely than patients in the control group to be treated in a private hospital (χ^2=251.8, df=1, p<0.001). In fact, 98.1% of all DBS procedures were performed in the private sector. There were no patients in the control group who had DBS.

Overall patients with PD were approximately twice as likely than controls to have a hospital admission for falls/fractures (19.8% vs 8.6%), dementia (14.4% vs 5.1%), psychiatric illness (13.6% vs 7.9%), gastrointestinal complications (diverticular disease/constipation/dysphagia) (13.3% vs 6.5%), syncope/orthostatic hypotension (11.5% vs 3.8%), genitourinary infections (10.6% vs 4.6%), encephalopathy/delirium (10.3% vs 1.8%), reduced mobility/motor fluctuations (10.1% vs 4.5%), pneumonia (9.8% vs 5.5%), spinal pain (5.5% vs 3.0%), adverse drug events (5.1% vs 1.7%), other trauma (4.3% vs 2.0%) (all p<0.001), sleep disorders/restless legs syndrome (1.8% vs 1.4%, χ^2=4.9, df=1, p=0.026), venous thromboembolism (1.4% vs 0.9%, χ^2=7.0, df=1, p=0.008) and electroconvulsive therapy (0.8% vs 0.4%, χ^2=11.4, df=1, p=0.001, table 3). By comparison, the patients with PD had proportionally fewer admissions in which there was a record of cardiac disease (16.7% vs 24.0%), neoplasia (7.3% vs 18.4%) and chronic airways disease (2.9% vs 7.2%) (all p<0.001). There was no difference in the proportions of each group who were recorded as having management of anaemia and stroke/TIA (table 3). Within the patient subgroup with a record of any neoplasm, there were fewer patients with melanoma in the PD group than the control group (0.25% vs 0.51%, χ^2=5.9, df=1, p=0.015).

Patients with PD as a principal diagnosis were approximately ten times more likely to have DBS recorded during their admission than patients with a secondary diagnosis of PD (41.1% vs 3.6%, table 4). By comparison, patients with a secondary diagnosis of PD had higher levels of falls/fractures (24.1% vs 8.6%), cardiac disease (21.7% vs 3.8%), dementia (16.8% vs 8.1%), gastrointestinal complications (15.4% vs 7.9%), syncope (13.5% vs 6.3%), pneumonia (12.5% vs 2.8%) and neoplasia (9.6% vs 1.3%) (table 4). Significantly more patients with a secondary diagnosis of PD had electroconvulsive therapy during their admission than those with a principal PD diagnosis (1.1% vs 0.1%, χ^2=14.5, df=1, p<0.001). Interestingly, reduced

Table 2 Clinical and demographic characteristics during acute care admission of PD patients, NSW 2008–2012 by principal PD diagnosis or secondary diagnosis

	Principal PD diagnosis	Secondary PD diagnosis	Test statistic	p Value
Number of patients (n=)	1574	4063		
Age (years) [SD]	68.2* [11.1]	77.6† [9.5]	t=−31.7 (5635)‡	<0.001
Gender (%)			χ^2=0.2 (1)§	0.619
Male	63.3	62.6		
Female	36.7	37.4		
Marital status (%)			χ^2=205.5 (3)§	<0.001
Married/de facto	73.6	58.6		
Widowed	8.5	22.9		
Single	10.2	9.9		
Other	7.7	8.6		
Hospital type (%)			χ^2=253.7 (1)§	<0.001
Public	9.6	29.9		
Private	90.4	70.1		
Average length of stay (days)			U test=3 411 066.0 (1)¶	<0.001
Median	6	7		
Interquartile ranges	3–11	2–14		
>20 days (%)	6.7	14.5		
Means of admission (%)			χ^2=528.9 (2)§	<0.001
Emergency	12.0	42.2		
Non-emergency/Planned	82.2	49.2		
Other	5.8	8.6		
Mode of separation (%)			χ^2=215.5 (3)§	<0.001
Discharge by hospital	83.7	63.9		
Transfer to other hospital	6.4	16.2		
Transfer to nursing home	3.5	6.7		
Death	1.7	4.4		

*Range (30–95 years).
†Range (33–100 years).
‡(Independent sample t test).
§(Pearson's χ^2 test).
¶(Mann–Whitney U test) df (degrees of freedom).
PD, Parkinson's disease.
Bold text signifies statistical significant results.

mobility/motor fluctuations were recorded as a diagnosis in approximately 10% of the patients in both these groups (table 4).

Logistic regression models were developed to further evaluate the significance of differences between the total PD and control groups for specific health problems during admission. Statistical significance persisted after controlling for age, gender, marital status, hospital type and LOS for differences in encephalopathy/delirium (Wald χ^2=310.0, df=5, p<0.001), adverse drug events (Wald χ^2=114.4, df=5, p<0.001), falls/fractures (Wald χ^2=431.5, df=5, p<0.001), dementia (Wald χ^2=410.1, df=5, p<0.001), pneumonia (Wald χ^2=111.3, df=5, p<0.001), syncope/orthostatic hypotension (Wald χ^2=265.8, df=5, p<0.001), neoplasia (Wald χ^2=315.2, df=5, p<0.001) and reduced mobility (Wald χ^2=201.7, df=5, p<0.001).

DISCUSSION

In our large population-based study, we identified many clinically important issues that are experienced more frequently by patients with PD than other patients. Hospitalisations for patients with PD in NSW occurred more often in the private sector, more frequently in men and those in a married or de facto relationship and were associated with a longer hospital stay than patients in the control group. In this study, we found that a greater proportion of the PD patients were treated in hospital following a planned admission and more of these patients were transferred to other hospitals or nursing homes postdischarge. Patients with PD receiving treatment in hospital had higher levels of reported health problems than controls for falls/fractures, dementia, DBS, psychiatric illness, gastrointestinal complications, syncope/orthostatic hypotension, genitourinary infections, encephalopathy/delirium, reduced mobility/motor fluctuation, pneumonia, spinal pain, adverse drug events, other trauma, sleep disorders/restless legs syndrome, venous thromboembolism and electroconvulsive therapy. However, patients with PD had a lower proportion of cardiac diseases, neoplasia and chronic airways disease than controls and the frequency of anaemia and stroke/TIA was comparable between the two groups.

The results of the present study are similar to those from other international studies, which found that admissions for falls, mobility complications, pneumonia, psychiatric problems, genitourinary infections and trauma were more prevalent among patients with PD than controls.[9 12 15 16 20] Previously identified common reasons for hospitalisation of patients with PD worldwide were also identified in our study.[8–12 16 20–24] From an Australian perspective, we found higher levels of morbidity in patients with PD with regards to admission for falls/fractures, cardiac disease, syncope, gastrointestinal complications, urinary disorders, dementia and encephalopathy than

Table 3 Health problems during acute care admission of PD and control patients, NSW 2008–2012

	Total Parkinson's patients	Control	χ^2 (1 df)	p Value
Number of patients (n=)	5637	8143		
Falls and fractures (%)	19.8	8.6	360.4*	<0.001
Ischemic heart disease/heart failure/ arrhythmia (%)	16.7	24.0	107.4*	<0.001
Dementia (%)	14.4	5.1	350.2*	<0.001
Deep brain stimulation (%)	14.1	0	1217.1*	<0.001
Psychiatric illness (%)	13.6	7.9	118.2*	<0.001
Diverticular disease/constipation/ dysphagia (%)	13.3	6.5	183.3*	<0.001
Syncope/orthostatic hypotension (%)	11.5	3.8	302.2*	<0.001
Genitourinary infections (%)	10.6	4.6	182.9*	<0.001
Encephalopathy/delirium (%)	10.3	1.8	475.8*	<0.001
Reduced mobility/on/off fluctuations (%)	10.1	4.5	165.1*	<0.001
Pneumonia (%)	9.8	5.5	90.4*	<0.001
Neoplasia (%)	7.3	18.4	344.2*	<0.001
Anaemia (%)	5.9	5.7	0.3*	0.563
Spinal pain (%)	5.5	3.0	54.6*	<0.001
Adverse drug event (%)	5.1	1.7	123.8*	<0.001
Other trauma (%)	4.3	2.0	61.3*	<0.001
Stroke/TIA (%)	3.9	4.0	0.1*	0.740
Chronic airway disease (%)	2.9	7.2	118.4*	<0.001
Sleep disorders/restless legs syndrome (%)	1.8	1.4	4.9*	0.026
Venous thromboembolism (%)	1.4	0.9	7.0*	0.008
Electroconvulsive therapy (%)	0.8	0.4	11.4*	0.001

*(Pearson's χ^2 test) df (degrees of freedom).
PD, Parkinson's disease.

previously described.[10] Our sample not only reflected the experience of patients in the larger cities but also included patients hospitalised across regional and rural areas who tend to be older and are diagnosed at a later age than patients from metropolitan areas.[25] These characteristics may be reflected in higher levels of age-related complications experienced during hospitalisation by patients in this sample and this, in turn, may have influenced their higher levels of morbidity. Further, the patients in our study had a shorter hospital stay than reported in other groups.[9 23] This may be a reflection of the more integrated approach to hospital care in Australia for patients with PD, which aims to incorporate the early use of allied health and acute medical units.[26 27] Alternatively, it may be a reflection of the slightly higher proportion of planned admissions in our PD group.

We found that there were a number of health problems in this patient group that have been previously unrecognised in other surveys of patients with PD. In our sample, patients with PD were five time more likely to be treated for delirium, three times more likely to experience an adverse drug event and syncope, more than twice as likely to require management of falls/fractures, dementia, gastrointestinal complications, genitourinary infections, reduced mobility and other trauma than compared with a control group weighted for the age and gender distribution of patients with PD in Australia. These problems should be considered major drivers for hospitalisation and healthcare in PD. We suggest that clinicians should focus on addressing the complexity of presenting problems and the complications associated with PD hospitalisations and that additional health resources should be allocated to assist them. Such efforts should include increased access to specialists by outpatients, which has been shown elsewhere to prevent unnecessary hospitalisations in PD,[11] as well as increasing the number of dedicated inpatient facilities akin to stroke units, in order to minimise adverse health outcomes and potentially reduce inpatient LOS. Further, it has been suggested that the quality of care during hospitalisation and patient motor outcomes could be improved by addressing preventable medication errors and allowing selected patients to take control of their own PD medication.[28] This is because non-neurology admitting teams, including nursing staff without PD training, may not be as familiar with the time criticality of PD medications, especially in patients with motor fluctuations.

Interestingly, we were able to report that patients with PD were half as likely to require hospitalisation for chronic airways disease and neoplasia, with significantly lower rates of in-hospital management of melanoma than in controls. The differences between the two groups with regards to neoplasia treatment persisted even after controlling for age and gender differences. Smoking prevalence has been shown to be lower in patients with PD,[29] likely limiting the risk of developing smoking-related cancers.[30 31] The lower rates of admission of patients with PD for treatment of chronic airways disease found in this study may be a reflection of lower smoking rates in this

Table 4 Health problems during acute care admission of PD patients, NSW 2008–2012 by principal PD diagnosis or secondary diagnosis

	Principal PD diagnosis	Secondary PD diagnosis	χ^2 (1 df)	p Value
Number of patients (n=)	1574	4063		
Falls and fractures (%)	8.6	24.1	172.7*	<0.001
Ischemic heart disease/heart failure/arrhythmia (%)	3.8	21.7	263.1*	<0.001
Dementia (%)	8.1	16.8	68.7*	<0.001
Deep brain stimulation (%)	41.1	3.6	1311.3*	<0.001
Psychiatric illness (%)	9.3	15.3	33.8*	<0.001
Diverticular disease/ constipation/dysphagia (%)	7.9	15.4	55.2*	<0.001
Syncope/orthostatic hypotension (%)	6.3	13.5	57.5*	<0.001
Genitourinary infections (%)	5.7	12.5	54.4*	<0.001
Encephalopathy/delirium (%)	5.0	12.3	65.7*	<0.001
Reduced mobility/on/off fluctuations (%)	9.0	10.5	3.1*	0.078
Pneumonia (%)	2.8	12.5	120.2*	<0.001
Neoplasia (%)	1.3	9.6	114.2*	<0.001
Anaemia (%)	1.7	7.6	71.1*	<0.001
Spinal pain (%)	3.3	6.3	19.7*	<0.001
Adverse drug event (%)	3.1	5.9	18.8*	<0.001
Other Trauma (%)	1.5	5.4	43.4*	<0.001
Stroke/TIA (%)	1.1	4.9	43.6*	<0.001
Chronic airway disease (%)	0.8	3.7	35.6*	<0.001
Sleep disorders/restless legs syndrome (%)	1.0	2.2	9.3*	0.002
Venous thromboembolism (%)	0.4	1.8	14.8*	<0.001
Electroconvulsive therapy (%)	0.1	1.1	14.5*	<0.001

*(Pearson's χ^2 test) df (degrees of freedom).
PD, Parkinson's disease.

PD population. Overall cancer risks have been shown to be lower in PD compared with control populations,[30 32] despite evidence that suggests that patients with PD are more likely to develop melanoma.[30 33] Past case reports have speculated that there may be a positive association between levodopa use and melanoma risk,[34] but these associations are largely unverified and remain controversial. The patients with PD in this study had lower levels of cardiac disease than the control group, which is consistent with the results from previous analyses.[15 20]

In our PD patient sample, we identified that 14.1% of the patients received hospital treatment for DBS management, of which more than half were new insertion procedures. Patients were significantly more likely to receive DBS if they were younger, married and were treated in a private hospital. DBS is well regarded as an important treatment option for patients with advanced PD.[35 36] Across tertiary medical centres, DBS surgery is usually considered a leading cause for elective hospitalisation in patients with PD.[9] Surgical, as well as hardware-related complications, are also known to occur in this group of patients, in addition to the recognised complications of medical therapy during a hospitalisation.[37]

We used hospital administrative data to examine patterns of morbidity in patients with PD. While these data provide very valuable information, they have some limitations. These include the possibility that there may be misclassification of patients with other causes of PD into the group classified as idiopathic PD used in this study. In addition, the data are in the form of unmatched patient records, and, therefore, it is not possible to identify multiple admissions for individual patients in this analysis. Administrative underreporting of patient comorbidities at the time of patient discharge may have underestimated the number of associated diagnoses attributed to an admission. However, this problem may be minimised by the activity-based funding used in the Australian healthcare system. In addition, the large sample sizes in this study may have contributed to the high levels of statistical significance identified in many of the comparisons. For this reason, we have chosen to focus on the clinical importance of the observed differences. In addition, we used regression models to explore the relationships between admissions after controlling for demographic differences and comorbidities between the sample groups. Lastly, the reduced LOS in the control group compared with the PD group may reflect a different distribution of health problems and their treatments, where patients with PD may use fewer short stay preventive or therapeutic procedures, such as colonoscopies and cataract surgery, compared with non-PD patients.

CONCLUSION

Our study identified differences in the demographic characteristics, health problems and treatments in hospital between patients with PD and a control group of patients without PD. Patients with PD had a considerably higher proportion of hospitalisations with problems, including delirium, adverse drug events, syncope, falls/fractures, dementia, gastrointestinal complications, genitourinary infections, reduced mobility and other trauma. These findings highlight the need for prehospital management and prevention of these issues through specialist clinics as well as primary care. We suggest that clinicians in hospitals should identify those patients at risk of complications early and work with multidisciplinary teams to ensure complications are minimised. Gait and balance assessments, adopting falls prevention strategies, early swallowing and speech therapy reviews, nutritional and dietary support, education on the common adverse drug events in PD, as well as timely administration of medication would be of benefit to the hospitalised PD patient. Further studies investigating risk factors for hospitalisation such as those by Hassan *et al*, identifying the effects of disease severity, patient comorbidities and DBS on hospital encounters,[38] are vital for informing clinicians about strategies to avoid preventable admissions.

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5.0 CHAPTER 5 – METHODS

5.1 Study And Comparison Samples

The NSW Ministry of Health maintains a database, the Admitted Patient Data Collection (APDC), on all separations from public and private hospitals in NSW. All admission diagnoses are grouped according to the ICD-10 AM (International Classification of Diseases, Tenth Revision) Chapter headings. (60) In this study, all patients with either a principal diagnosis of Parkinson's disease or a co-morbidity recorded as Parkinson's disease (ICD-10-CM G20) who were separated from a NSW hospital (public or private) between the years 2008 and 2012 were included in the study sample.

Demographic and clinical characteristics of patients in the study sample were compared to those of a comparison group, which was comprised of a randomly selected sample of inpatients who did not have a code for Parkinson's disease in any diagnostic field and was weighted according to the age and gender profiles of patients with Parkinson's disease in the Australian population. (21) An in-depth discussion of the difficulties in selecting the comparison group is provided below in Chapter 6, section 6.2.

As the data was non-identifiable, with no patient names or addresses included, no patient consent was obtained. The study was approved by the University of Notre Dame, Human Research and Ethics Committee.

5.2 Inclusion / Exclusion Criteria

A number of inclusion and exclusion criteria were used to select a subset of admissions into the final samples that were used in the analysis.

5.2.1 Parkinson's Disease Patients

All patients separated from a NSW hospital (public and private) between 2008 and 2012 with a diagnosis of Parkinson's disease (Idiopathic Parkinson's disease (ICD-10-CM G20)) as either the principal diagnosis or as a co-morbid diagnosis were selected into the study sample.

5.2.2 Random Sample Comparison Group

A randomly selected sample of patient records relating to admissions for any principal diagnosis other than Parkinson's disease and without any recorded co-morbid diagnosis of Parkinson's disease in 2008, representing 25% of all the admissions in that time period, was chosen as the comparison group. This sample selection was weighted according to the age and gender distribution of the most recent prevalence data of Parkinson's disease in Australia. (21) The gender ratio was 1.10:1, male to female respectively. (21)

The proportions of each age group in comparison sample were: 6 % - < 55 year olds, 12 % - 55-64 year olds, 29% - 64-74 year olds, 33% - 75 – 84 year olds, and 20% - > 85 year olds.

5.2.3 Exclusion Criteria (Cases)

Admissions with other diagnoses of Parkinsonism, including atypical Parkinson's disease, secondary Parkinson's disease or Parkinson's Plus Syndromes were excluded. Patients admitted for the purposes of inpatient rehabilitation, psychiatric treatment and dialysis were also excluded.

5.3 Sample Size Calculation

A power calculation determined that a sample size of 480 in each group (Parkinson's disease patients and comparison sample) would have 80% power to detect a difference of 20% for a

given outcome variable (yearly admissions with pneumonia in Parkinson's patients versus comparison sample) between the groups with an alpha level of 0.05.

5.4 Clinical Features For Investigation

The data requested from the APDC from the NSW Ministry of Health are described below. The subjects for inclusion in the study sample were defined as having idiopathic Parkinson's disease as principal or co-morbid discharge diagnosis from any admission to a NSW public or private hospital from all admissions between 2008-2012 inclusive. The demographic variables that were included were: age, sex, marital status, health insurance status and country of birth. Admission details were also requested, which included: length of admission (inpatient stay), and whether the patient was classed as a private or public admission. The type of admission was also requested, including whether the admission was elective (planned); through an Emergency Department; whether it was a readmission (defined as less than two weeks from discharge from hospital).

The reasons for admission for both a principal and secondary diagnosis of Parkinson's disease were also requested. Variables of significant clinical interest included: motor complications / reduced mobility, falls / fractures, pneumonia / aspiration pneumonia, cardiac issues / acute myocardial infarction / heart failure, syncope / orthostatic hypotension, genitourinary infections, gastrointestinal issues / constipation, encephalopathy / delirium / drug induced psychosis / psychosis, cancer / neoplasia, stroke / transient ischemic attack, dementia without psychosis, elective surgery / Deep Brain Stimulation, haematological disorders, venous thromboembolism / pulmonary embolism / deep vein thrombosis, chronic airflow limitation / chronic obstructive pulmonary disease, psychiatric problem / depression / anxiety, sleep disorders / restless leg syndrome, spinal arthritis / back pain, general medical problems, miscellaneous admissions and day procedures.

Treatment options including, use of Electroconvulsive Therapy during inpatient stay as well as Incident Information Management System / errors / notifications / medication errors during

admission. Surgical procedures performed during admission including, all coded procedures available, of clinical interest: Deep Brain Stimulation.

Allied Health accessed: Physiotherapist, Speech Pathologist and Occupational Therapist.

Discharge destination: inpatient / in hospital death, transfer to other hospital, inpatient rehabilitation, nursing home, home, other.

5.5 Development Of A Clinical Diagnosis From The International Classification of Diseases

From these ICD-10 Chapter headings, (60) our research project required appropriate clustering of diagnoses according to the clinical conditions related to Parkinson's disease. As an example, cardiac diseases included myocardial infarction (I21) and conduction disorders (I44). Orthostatic hypotension (I95) and syncope and collapse (R55) were classified individually due to their specific relevance to Parkinson's disease. Deep Brain Stimulation insertion was represented by procedure codes: 92036 (insertion of intracranial electrode via burr holes) and 39138 (insertion of intracranial electrode via craniotomy).

ICD coding also was able to demonstrate the type of allied health utilisation patients encountered during the admission, if any. Common ICD procedure codes for allied health intervention included, Physiotherapy (95550-03), Speech Pathology (95550-05) and Occupational Therapy (95550-02).

5.6 Statistical Analysis

The statistical analysis for this project was conducted using the SPSS – 20 software package. (61). A number of statistical approaches were undertaken as part of a very comprehensive analysis of the data. The results are presented as frequencies for dichotomous variables and as means or medians for continuous variables. Differences in the distribution of continuous variables between the groups were assessed using the two-sample t test for independent

variables. Where the data were highly skewed, such as the length of the inpatient stay, the Mann–Whitney U test was used to compare the distribution of the particular variable between the groups. χ^2 tests were used to compare differences between categorical variables.

5.7 Statistical Modelling

Statistical modelling was undertaken to explore differences in admission outcomes for patients with Parkinson's patients as a primary diagnosis compared with patients whose Parkinson's patients was recorded as a secondary diagnosis. A similar approach was also used for patients in the Parkinson's patient group compared with patients in the comparison sample. The modelling allowed for determination of the influence of a number of predictor variables considered simultaneously on the outcome under consideration. In particular, the modelling was used to assess whether the effect of a particular variable persisted after controlling for the effect of other factors, such as age, gender, marital status, hospital type and LOS, on the outcome of interest. A 5% level of significance was used for all analysis within our study.

5.7.1 Purpose Of Statistical Modelling And Consideration Of The Model

Where several variables were significantly associated with the outcomes of interest in the study on bivariate analysis, statistical modelling was used to determine the effect of each of these variables after controlling for the effect of other variables that were predictive of a particular health outcome. As the outcome variables were dichotomous, logistic regression models were developed. To assess the influence of comorbidities on these outcomes, other predictor variables (such as age and sex) were forced into the model. The decision to include each comorbidity variable at each step was based on the Wald statistic, with $p < 0.05$ chosen as the cut off for statistical significance.

A series of logistic regression models were also constructed to evaluate differences in the presence of various health problems between the entire Parkinson's disease sample and the

comparison group. Models investigated differences in a number of comorbidities, after controlling for the demographic variables including age, gender, marital status, hospital type and LOS.

5.7.2 Logistic Regression

The logistic method assumes that for each observation, the outcome variable is dichotomous and can take the value of 1 or 0 ("success" or "failure"). If we let μ represent the probability of "success" then the logit of μ (the log odds of "success") can be expressed as a linear combination of the explanatory variables. For p explanatory variables ($\chi_{1,\ldots,}\chi_p$), the model has the form:

$$\log (\mu / (1-\mu) = \beta_0 + \beta_1\chi_1 + \beta_2\chi_2 + \beta_3\chi_3 + \ldots + \beta_p\chi_p$$

where the coefficients ($\beta_{0,\ldots,}\beta_p$) represent the coefficients to be estimated. The error distribution is assumed to be binominal.

6.0 CHAPTER 6 – DISCUSSION

6.1 Introduction

This chapter will present and evaluate the new information that was obtained from this investigation on hospitalised Parkinson's disease patients in Australia. It will review the clinical significance of the results and reflect on the strengths and weaknesses of the study. It will address aspects of the study design and analysis, as well as consider the analytic and computational challenges encountered in the evaluation of comorbidities of Parkinson's disease patients. Finally the implications of common adverse drug events for Parkinson's disease patients are discussed and the association between DBS and hospitalisation is reviewed.

The results of this Master's project provide insight into the importance of neuro-epidemiological research into Parkinson's disease in Australia. This research gives new insights into the reasons for hospitalisation of patients, particularly with regards to the dramatically higher proportion of patients with Parkinson's disease being hospitalised for delirium; adverse drug events; syncope; and falls/fractures compared to those from the comparison sample. Further, the burden of important comorbidities among Parkinson's disease patients has also not been evaluated extensively, particularly in the Australian setting. Many of our study's findings were novel and have not been previously described. The research described the important and clinically significant findings that were identified in the large dataset of Parkinson's disease patients, which were informed by a review of the literature, and were compared to a reference population. This included important demographic features relating to length of stay, means of admission and separation, as well as comorbidities associated with the need for hospitalisation.

The conclusions drawn from the study could be used to inform the planning of health services by local and state health authorities, particularly emphasising the need for improved access to outpatient clinics to avoid unnecessary hospitalisations for the most frequent causes of Parkinson's disease hospitalisation. Unfortunately there is a paucity of evidence that such

dedicated outpatient clinics currently minimise admission rates for patients with Parkinson's disease within Australia. Accordingly, a follow on study could be beneficial to examine such a hypothesis. Further, the results from our study could also be used to adjust current Activity Based Funding for hospitalised Parkinson's disease patients. Finally, this study's findings could be utilised to support financial provisions for services aiming to offer strategies to minimise the length of stay of patients with Parkinson's disease.

6.2 Study Design

A descriptive analytic design based on a cross-sectional sample of patients with Parkinson's disease and comparison sample of patients without Parkinson's disease was chosen to address the aims of the study. The study was strengthened by the inclusion of admissions to all hospitals (both public and private) in NSW over a number of years, making it large and population-based. Of particular relevance was that the study considered patients who had either a principal diagnosis or a comorbid diagnosis of Parkinson's disease (which is important because a patient may have had an alternate major problem, such as a pneumonia but the Parkinson's disease may have predisposed the patient to pneumonia). In addition, the diagnoses used in this analysis were made by medical practitioners, rather than from than from patient self-reports. This is likely to lead to a more accurate classification of patients and is preferable to the methods used in other studies of Parkinson's disease. (62, 63) Further, the study included a normative sample from the general patient population without Parkinson's disease, which was selected using a random sampling technique and was weighted according to the age distribution of patients with Parkinson's disease in the source population.

However, there were a number of potential weaknesses in the study design. First, it is likely that there were patients who were hospitalised and had Parkinson's disease but who were not identified as having Parkinson's disease in the discharge summary and, therefore, were not included in the study. The extent to which this occurred could not be determined in this analysis and is, therefore, unknown. However, it is probable that this phenomenon is more likely to be an issue for patients with milder disease rather than those with more severe

Parkinson's disease. In addition, it is possible that patients with a Parkinson's disease diagnosis in the discharge summary may not have been coded as having Parkinson's disease in the APDC or may have been miscoded as Parkinson's disease but this is likely to be much less common than patients with Parkinson's disease remaining unidentified by the clinicians managing the patient. This assumption is supported by the rigorous auditing procedures that are undertaken at both the hospital and departmental level in which the accuracy of coding of the diagnoses documented in the discharge summary is assessed. In addition, patients may have been included more than once in the dataset. This is because the records were not linked and individual patient histories could not be identified. This effect may vary depending on the severity of the patient's illness, where the patients who had more severe illness may have had more frequent readmissions than patients whose disease was less severe. Patients may also have been excluded from the dataset if they sought treatment in alternate states/territories. This is particularly likely among patients living near state borders, and it is likely that the converse may also apply, whereby patients from nearby states/territories may have sought treatment in NSW. In this analysis, the in-hospital mortality rate was determined but it was not possible to estimate the number of deaths that occurred outside the hospital environment.

In this study, it was not possible to ascertain whether there was an under-recording or over-recording of a patient's diagnosis as Parkinson's disease, either as a primary diagnosis or co-morbidity, due to an error by the clinician or hospital coding staff. In addition, given the complexities of making a diagnosis of idiopathic Parkinson's disease, it was not possible to verify its accuracy and it is possible that the accuracy varied between sites depending on the availability of specialist staff. This could be reflected in the possible under-reporting of the Parkinson's disease hospital separations in this study, as these comprised only 0.04% of the admissions in our source population but there are estimates from other studies that the prevalence of Parkinson's disease in Australia is higher, and was found to be 0.46% in the Blue Mountains Study, (53) and approximately 0.3% in an Access Economics Report. (21)

Activity Based Funding (and therefore, financial incentive for increased diagnoses) was introduced mid-way through the study period, and it is unknown whether this led to an increase in recording of Parkinson's disease as a comorbidity in the APDC. In an attempt to verify true Parkinson's diagnoses, we initially planned to assess medication lists, looking for

typical Parkinson's disease medications such as L-dopa based treatments and dopaminergic agonists to validate a probable Parkinson's disease diagnosis. Unfortunately, this data was not available from the Ministry of Health, thus this validation of the recorded diagnosis of Parkinson's disease could not be conducted.

Other potential weaknesses in our study design were related to the selection of a suitable comparison sample group. This included the need to exclude certain types of hospitalisations (rehabilitation, psychiatric and dialysis services), given their varied length of stay, and types of treatment offered during such admissions. Regarding the normative population sample, various logistical issues existed within the Ministry of Health. In the database, public and private datasets are maintained separately, making it difficult to generate a sample group over the 5-year study period. Accordingly, a representative sample of patients from a single year, 2008, was used. The same exclusion criteria were applied to the comparison sample as the Parkinson's disease sample, however is was apparent that a higher proportion of patients in the control group had shorter hospital stays, often one-day admissions for day procedure cases. This notion was supported by the difference in median LOS between the groups, 7 for Parkinson's disease and 1 for the control group. We decided against imposing further exclusion criteria on the comparison sample (for instance, eliminating day procedures), we believe this would negatively impact on the generalizability of the results. We hope to address this problem more effectively in subsequent planned analyses, as discussed in Future Directions. One strategy would be to exclude all patients from both groups who were admitted for day procedures.

A potential bias within our study design could also result from the lack of homogeneity in the proportions of patients in our dataset, with regard to the proportions of public and private hospitalisations, as well as emergency and planned admissions. It is probable that such a variety of differing presentation types reflected differing models of care available to patients, resulting in potentially more unwell patients being managed through the public system and presenting through Emergency Departments and perhaps more elective/planned admissions resulting in slower stream medical/rehabilitation care being managed in the private system.

Approximately three-quarters of the Parkinson's disease patients in our study were admitted to private hospitals. It is plausible that there were different services available in the private and public sectors, including the availability of allied health interventions as well as procedures, such at DBS, which was overwhelmingly found in private hospital admissions. These differences may have impacted on outcomes such as LOS, as well as accounting for some differences in complications arising during admission, including delirium, adverse drug events, syncope and falls/fractures. A sub-group analysis of private versus public patients or emergency versus elective admissions could have been considered to further evaluate potential management differences, however it was considered outside the scope of the current project but could be considered in further analyses.

6.3 Study Analysis

A variety of statistical tests were performed in the analysis of our data with the aim of providing a clear understanding of the comparison between our Parkinson's disease patients and the comparison group. T-tests and chi-squared tests were used for comparison of continuous and nominal demographic and diagnosis related data respectively. The ability to demonstrate patterns in admissions in a substantial proportion of our data analysis through these tests was a significant strength to our data analysis.

There were however substantial differences in the distribution of the variable LOS between groups and for this reason a non-parametric test was utilised to assess the median difference in LOS, accompanied by interquartile ranges for comparison. Adjustment for multiple pairwise tests is undertaken in some studies and is a valid approach for dealing with multiple comparisons, however, this was not conducted in this analysis.

Logistic regression modelling was performed to explore the relationships between the groups of interest (patients with Parkinson's disease and the comparison group) and a series of dichotomous outcome variables. This is the appropriate choice of model in this situation and allows for estimations of effect after controlling for differences in demographic features and

comorbidities between the sample groups. The rationale employed in developing the logistic regression models aimed to demonstrate which of a number of observed bivariate associations was significant, after controlling for the associations of all variables in the model with the outcome of interest. This allowed for the control of demographic characteristics (including age, gender, marital status, hospital type and LOS) while assessing the effect of a predictor variable. Importantly, it was identified that encephalopathy/delirium, adverse drug events, falls/fractures, dementia, pneumonia, syncope/orthostatic hypotension, neoplasia and reduced mobility admission were significantly more common in the Parkinson's disease population than in the comparison group, after controlling for the differences in demographic characteristics between the two samples. These findings from the logistic modeling strengthened our study's comparative analysis.

6.4 Patient Comorbidities

An interesting observation from our study was the relationship between Parkinson's disease and vascular disease co-morbidities, particularly relating to stroke and heart disease. We identified that our cohort of Parkinson's disease patients had fewer admissions for ischemic heart disease / heart failure or arrhythmia than the control group, 16.7% versus 24.0%, but no difference in stroke hospitalizations (3.9% versus 4.0%). The exact reason for this observed effect is not entirely clear, as other worldwide studies have also suggested that cardiovascular disease rates were lower in patients with Parkinson's disease. (14, 38) If, indeed, there was an overall difference between the Parkinson's disease population and the control group in the prevalence of systemic vascular disease, then stroke rates would also be expected to be lower in the Parkinson's disease than the comparison group. However this effect was not found.

One reason for the observed differences in ischemic heart disease admissions may be that there are lower smoking rates in Parkinson's disease. (64) This assumption may be reinforced by the fact that there were significantly fewer admissions for chronic airways disease in the Parkinson's disease than in the comparison group, 2.9% versus 7.2%. However it is probable that other confounders such as other lifestyle factors including exercise and diet, medications such as antihypertensives, lipid lowering treatment and control of diabetes could all have an

impact on this result. Unfortunately, these variables were not available in the dataset for analysis.

A final interesting difference in the distribution of comorbidities that we observed was the subgroup difference for melanoma hospital admissions. Previous studies, although controversial and of lower quality, have indicated that melanoma rates are slightly increased in the Parkinson's disease population compared to the general population, and they have hypothesized that this may be related to levodopa use. (65) This notion was not reflected in our analysis, where 0.25% of the Parkinson's disease hospitalizations compared with 0.51% of the comparison sample hospital admissions had a diagnosis of melanoma. This apparent difference could suggest that there was significant under reporting of melanoma comorbidities for Parkinson's disease patients, or possibly that access to treatment for skin disease / skin cancer during a hospitalization may be different between Parkinson's disease and control group patients. A plausible reason for the lower levels of hospitalization for melanoma among Parkinson's disease patients could not be suggested outside of the usual sun-avoidance measures and patient infirmity.

6.5 Adverse Drug Events

An important finding of our analysis was that adverse drug events were significantly higher in the Parkinson's disease population than the comparison group. This has important implications, given that many patients with Parkinson's disease usually require a strict time-dependant administration of dopamine replacement medication to control their motor symptoms. Issues relating to incorrect administration / timing of patients' regular medication, omission of doses or, importantly, drug interactions with other classes of medications, particularly dopamine blocking agents, can have profoundly adverse side effects. These can negatively influence Parkinson's disease patients' welfare and predispose them to increased complications that may lead to prolonged periods of hospitalisation. We found that the most frequent adverse drug events included: confusion, dystonic / extra pyramidal effects, postural hypotension, anticholinergic events, sedation and drowsiness and gastrointestinal disorders. It has been argued that perhaps an effective measure for reducing in-hospital medication related

side effects could be achieved by allowing selected patients to take control of the administration of their own Parkinson's disease medications. (66)

6.6 Deep Brain Stimulation And Its Effects On Hospitalisation.

There has been recent research on the effects of DBS in Parkinson's disease, with regard to the investigation of potential differences in modifying strategies to minimise adverse outcomes, differences in length of stay, and determination of the improvements in the quality of life of Parkinson's disease patients. (67, 68) With increasing numbers of patients gaining access to DBS across the world, more detailed studies are now available on the types of complications that arise from initial device implantation as well as the provision of follow up care. (69, 70)

A recent Portuguese study analysing long-term mortality in DBS in 184 patients, followed up patients for a mean of 50 months. It showed that 15 deaths occurred during the study, (total 8.15%, expected annual mortality rate 1.94%), (71) inferring that these rates were comparable or perhaps even lower than those receiving best medical therapy. (71-73) This may be a reflection of improved motor control leading to fewer complications such as falls and fractures in addition to increased medical surveillance of Parkinson's disease patients with DBS, prompting earlier consideration to changes in management. Further analysis of DBS patients showed that the most common causes of mortality included stroke, myocardial infarction, other vascular/heart disorders, or severe infection, with one suicide being recorded. (71) These patients' morbidities were quite similar to those identified in our study, however we were not able to discern the actual causes of death during hospitalisation due to lack of appropriate data-linkage. Overall it has been shown that DBS survival rates exceed 99% and 94% at 3 and 5 years respectively. (71, 72)

Further, an analysis of DBS Parkinson's disease cohorts across various centres within the United States of America suggest that patients with DBS may have improved healthcare outcomes in terms of minimized adverse events and complications as well as decreased

length of stay. (74) However, there were specific caveats noted within this study, with large volume, academic centres showing the most favourable results. Although the authors make recommendations supporting widespread availability of DBS across smaller, academic centres including those in rural areas, ultimately they highlight the importance of DBS providing easier access for patients to advanced Parkinson's disease treatment, as well as reducing the total cost of hospitalisation. (74)

6.7 Conclusion

Planning and subsequently analysing this large population study was a challenging yet rewarding project. Learning to incorporate bio-statistical methodology such as the use of a robust comparator group, large population sample and comprehensive yet straightforward data analysis was intrinsic to the aim for the study that was published in a highly reputable peer reviewed journal. These features were planned from the initial phases of the study and were continually reviewed to make sure the project delivered on its objective to provide a clear understanding to the reasons for hospitalisations of Parkinson's disease patients in NSW, as well as in-depth analysis of the comorbidities of hospitalised Parkinson's disease patients.

Various complexities including the composition of the comparison group, management of multiple ICD diagnoses into workable diagnostic groups and others mentioned above needed to be continually refined to enhance the analysis of the results and allow for logical conclusions to be drawn from the results.

7.0 CHAPTER 7 – CONCLUSIONS

7.1 Introduction

In this chapter, the conclusions and recommendations that follow from this study are discussed. Many of these were described in the publication in the JNNP, (75) which forms the main component of this Thesis. However, further recommendations are made with regards to practical measures that can be taken to prevent both unnecessary hospitalisations for patients with Parkinson's disease and to minimise the risk of adverse events among Parkinson's disease inpatients. These will be discussed in the following paragraphs. The remainder of the chapter covers a discussion of my learning experiences as a maturing researcher, in addition to recommendations for future research in this area, including the utilisation of record-linkage to examine the long-term outcomes of patients with Parkinson's disease.

7.2 Published Conclusions

The project's most significant results were firstly, that patients with Parkinson's disease had a considerably higher proportion of hospitalisations with complications, including delirium, adverse drug events, syncope, falls/fractures, dementia, gastrointestinal complications, genitourinary infections, reduced mobility and other trauma than patients in the comparison sample. Further, it was identified that hospitalisations for patients with Parkinson's disease in NSW occurred more often in the private than public sector. Hospitalisations also occurred more frequently in men and those in a married or de facto relationship and were associated with a longer hospital stay than patients in the comparison sample group.

In addition, a greater proportion of the Parkinson's disease patients were treated in hospital following a planned admission and more of these patients were transferred to other hospitals or nursing homes post discharge. Patients with Parkinson's disease receiving treatment in hospital had higher levels of a number of health problems than those in the comparison sample. These included falls / fractures, dementia, DBS, psychiatric illness, gastrointestinal

complications, syncope / orthostatic hypotension, genitourinary infections, encephalopathy / delirium, reduced mobility / motor fluctuation, pneumonia, spinal pain, adverse drug events, other trauma, sleep disorders / restless legs syndrome, venous thromboembolism and electroconvulsive therapy. However, patients with Parkinson's disease had a lower proportion of cardiac diseases, neoplasia and chronic airways disease than the comparison group and the frequency of anaemia and stroke / TIA was comparable between the two groups. Reassuringly, the results of the present study were similar to those from other international studies which found that admissions for falls, mobility complications, pneumonia, psychiatric problems, genitourinary infections and trauma were more prevalent among Parkinson's disease patients than controls.

Moreover, the Parkinson's disease patients in the study group had a shorter hospital stay than reported in other groups, internationally. (30) This may be a reflection of the more integrated approach to hospital care in Australia for patients with Parkinson's disease, which aims to incorporate the early use of allied health and acute medical units. Alternatively, it may be a reflection of the slightly higher proportion of planned admissions in the Parkinson's disease group in the Australian sample.

Following the analysis, a number of practical steps were recommended in an effort to improve health outcomes and reduce the number of unnecessary hospitalisations. These recommendations included highlighting the need for pre-hospital management and prevention of exacerbations of chronic comorbidities through better utilisation of specialist clinics and primary care. It was further suggested that hospital clinicians should identify patients at risk of complications early and work with multidisciplinary teams to ensure complications are minimised. Further recommendations addressing gait and balance assessments; adopting falls prevention strategies; early swallowing and speech therapy reviews; nutritional and dietary support; education on the common adverse drug events in Parkinson's disease; as well as timely administration of medication were proposed as means of potentially benefiting the hospitalised Parkinson's disease patient.

7.3 What I Have Learnt As A Maturing Researcher

Completion of this research project has provided valuable learning experiences for me in the analytical, research and clinical domains. It has provided me with an improved understanding of the importance of conducting sound epidemiological research into clinically important and relevant issues relating to a common neurological disorder and that frequently results in patient hospitalisation. Undertaking a literature review highlighted the issues related to hospitalised care for Parkinson's disease patients, whereas completing the analysis and developing discussion points in the article and thesis allowed me to further reflect on and challenge my understanding of the best way to manage and minimise complications for common causes of Parkinson's disease related hospitalisation. This has certainly had a positive impact on my future interest in continuing work in the field of neurodegenerative disorders, particularly Parkinson's disease, both in a clinical and research context. As a maturing researcher, I have tried to suggest useful recommendations that can positively influence Parkinson's disease patients' hospitalisations. As well, I have acknowledged the limitations, flaws and difficulties encountered in our study. These could either be addressed in further studies, or refined using our existing dataset with a view to providing further research into aspects of the epidemiology of Parkinson's disease in NSW.

7.4 Future Directions

The completion of this project had fostered future interest in developing other potential research directions in the neuro-epidemiology of Parkinson's disease. Research questions investigating the causes of death in previously hospitalised Parkinson's disease patients could provide invaluable new information on the health outcomes of patients with Parkinson's disease. This would best be achieved by developing a record-linkage project, which would match the hospital records of patients with the mortality files held by government agencies. There is a paucity of information on the long-term health outcomes of Parkinson's disease patients, including the causes of death in this patient group both in Australia and around the world. A comprehensive evaluation of such a dataset would be potentially beneficial for patients and their families.

Other potential areas of research include reviews of other types of hospitalisations, including sub-acute care and rehabilitation. As a significant proportion of patients with Parkinson's disease require rehabilitation focused medical care, either as the reason for an admission or following an episode of acute care, this type of analysis could also further inform the provision of rehabilitation services and their associated funding. Exploration of the patterns of utilisation of various allied health professionals, admissions for particular rehabilitation goals, overall and according to patient subgroups could be used to benchmark particular outcomes, such as length of stay, adverse events and discharge destinations.

It is hoped that, with the completion of the current and proposed research evaluating various clinical and epidemiological aspects of Parkinson's disease, a more comprehensive involvement with larger research groups both in Australia and overseas could be undertaken in movement disorders in the later years of my training.

APPENDIX 1 – ETHICAL CONSIDERATIONS

Human Research Ethics Committee approval has been granted prior to the commencement of the research project:

- University of Notre Dame, Sydney School of Medicine – HREC Approval: #013067S. Approved 16th May 2013.

Attached are:

- **HREC approval certificate**

- **Completed low risk application form requesting ethical clearance – UNDA HREC**

THE UNIVERSITY OF
NOTRE DAME
AUSTRALIA

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ABN: 69 330 643 210
CRICOS PROVIDER CODE: 01032F

16 May 2013

Dr Stephen Tisch
School of Medicine
The University of Notre Dame Australia
Sydney Campus

Dear Stephen,

Reference Number: 013067S

Project Title: "Parkinson's disease hospitalisations and co-morbidities: a retrospective cohort study of NSW patients."

Thank you for submitting the above project for Low Risk ethical review. Your application has been reviewed by a sub-committee of the university's Human Research Ethics Committee in accordance with the *National Statement on Ethical Conduct in Human Research* (2007). I am pleased to advise that ethical clearance has been granted for this proposed study.

All research projects are approved subject to standard conditions of approval. Please read the attached document for details of these conditions.

On behalf of the Human Research Ethics Committee, I wish you well with what promises to be a most interesting and valuable study.

Yours sincerely,

Dr Natalie Giles
Executive Officer, Human Research Ethics Committee
Research Office

cc: Prof Christine Bennett, Dean, School of Medicine Sydney;
Prof George Mendz, SRC Chair, School of Medicine Sydney.

THE UNIVERSITY OF NOTRE DAME AUSTRALIA

HUMAN RESEARCH ETHICS COMMITTEE

Application for Low Risk Review of a Research Project involving Human Participants

Important Information for Applicants

1. This application form is to be used by researchers seeking a Low Risk review for individual projects.
2. To find out if you are eligible for Low Risk Review, you should complete a Low Risk Review Checklist and refer to Section 2 of the National Statement regarding risk and benefit.
   Low Risk research describes research in which the only foreseeable risk is one of inconvenience and/or discomfort.
   In addition, if you are seeking a waiver of consent, you are required to fill in a Full Risk application form even if the foreseen risk is deemed "low".
3. Download a new form from http://www.nd.edu.au/research/hrec/apply.shtml to ensure that you are using the most current version of this form.
4. Handwritten applications will not be accepted.
5. Please respond **concisely** to all applicable sections, using **plain language** wherever possible.
6. Type an 'X' in checkboxes that apply.
7. Please also provide all necessary attachments where indicated.
8. The *National Statement on Ethical Conduct in Human Research (2007)* provides the primary guidelines for this application. This and other national guidelines can be found at http://www.nd.edu.au/research/hrec/links.shtml
9. University of Notre Dame research policies can be found at http://www.nd.edu.au/research/hrec/policies.shtml
   In particular read **Policy: Ethics Approval for Research Involving Humans** and **Guideline: Applying for Ethics Approval (Low Risk Clearance)**.
10. Your completed application must be submitted to your School Research Committee (SRC) for review together with the Low Risk Review Checklist. The SRC will then forward your application to the Research Office for HREC sub-committee review.
11. RESEARCH MUST NOT COMMENCE UNTIL WRITTEN APPROVAL HAS BEEN PROVIDED BY THE HREC SUB-COMMITTEE.
12. **Please note: The HREC may decide the application is not Low Risk and will therefore require a Full Review application or may find the study requires substantial changes prior to the commencement of the study.**
13. The HREC will not grant retrospective ethics approval.

THE UNIVERSITY OF NOTRE DAME AUSTRALIA

HUMAN RESEARCH ETHICS COMMITTEE

Application for Low Risk Review of a Research Project involving Human Participants

Registration No. *(HREC use only)* ☐☐☐☐☐☐☐

PROJECT TITLE:

Parkinson's disease hospitalisations and co-morbidities, a retrospective cohort study of NSW patients.

PROJECT SUMMARY:

[A plain English description of the project and its expected outcomes in no more than 100 words.]

There is a paucity of understanding to the reasons for admission and related co-morbidities of patients with Parkinson's disease during their hospitalisations. The aim of this study is to examine Parkinson's disease patient hospitalizations in regards to various demographics, co-morbidities as well as clinical management. In this study, data will be extracted from the NSW Ministry of Health, examining various coded patient admissions details over the last five years. Epidemiological, demographic and clinical features will be examined to assess for trends over time, as well as analysing potential correlations of patient co-morbidities that may have predisposed to their hospitalisation. The results of this retrospective study will be analysed to determine whether there are differences or correlations in various health outcomes for PD patients that lead to hospitalisation.

PROJECT TYPE

[Mark X to those that apply]

Staff Research Project		Student Research Project	
Project involving patients		PhD	Honours
Project involving students	X	Masters	Postgraduate Diploma
Funded consultancy		Undergraduate	Other Doctorate
Other *(describe briefly)*			

EXPECTED COMMENCEMENT DATE: 01.03.2013 **EXPECTED COMPLETION DATE:** DECEMBER 2014

SCHOOL/CENTRE:

[UNDA School which takes overall responsibility for this research project]

School of Medicine, Sydney

CHIEF INVESTIGATOR/SUPERVISOR: *[A UNDA staff member with ultimate responsibility for the research]*

Name	Dr Stephen Tisch		
Mailing Address	160 Oxford St, Darlinghurst. 2010. NSW		
UNDA Email	stisch@stvincents.com.au	**Phone**	02 8382 3305
Describe what the researcher will do in the context of this project.	Overall project supervisor, involved in the following roles: - Research Project: Conception and design, organization and execution - Statistical Analysis: Design, execution, review and critique - Thesis: Review and critique		

Describe the relevant experience the researcher has specific to this project.	Dr Stephen Tisch, MBBS PhD FRACP Staff Specialist, Department of Neurology, St Vincent's Hospital Consultant Neurologist, St Vincent's Private Hospital and Clinic. Area Of Interest: - Movement disorders - Deep brain stimulation - General neurology - Neurophysiology Leading expert in Movement Disorders including Parkinson's disease. Widely published in this area and maintains an active interest in research into the field. Has supervised in the past several research projects including a current University of Notre Dame, School of Medicine, student research project. Clinical interests in this project focus towards epidemiological analysis of Parkinson's disease.

CO- INVESTIGATOR/STUDENT:

Title and Name	Dr Michal Lubomski		
Address	1002/160 Goulburn St, Surry Hills. 2010. NSW		
UNDA Email	20084168@my.nd.edu.au	**Phone**	0410190830
Describe what the researcher will do in the context of this project.	Principle Researcher. Directly involved in all the project's activities, including the following: - Research Project: Conception and design, proposal submission and presentation, HREC approval, organization and execution - Statistical Analysis: Design, execution, review and critique - Thesis: Report writing, review and critique - Submission for publication		
Describe the relevant experience the researcher has specific to this project.	Dr Michal Lubomski, MBBS(Hons) Medical Resident, St Vincent's Hospital. Area Of Interest: - Movement disorders / Parkinson's disease - General neurology Completed an Honours Research year – 2011 as part of Medical training at University of Notre Dame. Research undertaken in a cross sectional clinic study of Parkinson's disease patients within Regional and Urban Victoria, Australia. Publication Jan 2013 – Journal of Clinical Neuroscience. Secondary manuscript examining Gender Clinical Characteristics of Parkinson's disease submitted for publication – March 2013. Movement Disorder Journal. Further interest in conducting a larger cohort study, focusing on epidemiological analysis of Parkinson's disease within Australia. The aim of this study is to further investigate the above clinical interest, a follow on of previous research conducted within this field.		

CO- INVESTIGATOR/STUDENT:

Title and Name	Associate Professor Louise Rushworth		
Address	160 Oxford St, Darlinghurst. 2010. NSW		
UNDA Email	louise@chrispassociates.com	**Phone**	02 8204 4404
Describe what the researcher will do in the context of this project.	Co-supervisor / Researcher. Involved project in the following roles: - Research Project: Conception and design, organization and execution - Statistical Analysis: Design, execution, review and critique - Thesis: review and critique		

Describe the relevant experience the researcher has specific to this project.	Associate Professor Louise Rushworth, MBBS (Hons), PhD, FAFPHM Professor of Clinical Epidemiology / Research. University of Notre Dame, School of Medicine. Area Of Interest: - Clinical Epidemiology of various chronic medical disorders. Previous co-author of Parkinson's disease cross-sectional publication with Michal Lubomski. Ongoing interest in clinical epidemiology across multiple disease states. Widely published across several medical fields, maintains an active interest in the research field. Has supervised many past students at University of Notre Dame, School of Medicine.

1. PROJECT DETAILS

1.1 KEYWORDS

Provide a list of, and definitions for, any technical terms and acronyms which may assist the HREC to understand this application.

TERM	LAY EXPLANATION
PD	Parkinson's disease

1.2 AIMS OF AND JUSTIFICATION FOR THE RESEARCH

State the aims and significance of the project. Where relevant, state the specific hypothesis to be tested. Provide a brief description of current research/literature review, a justification as to why this research is important and an explanation of any expected benefits to the community.

(Max 500 words)

This study has three aims. They are:

1. To examine the range of Parkinson's disease patient's hospitalisations in New South Wales over a 5 year period, to determine whether there are trends in patient demographics, reasons for admission as primary and secondary diagnosis, aspects relating to their clinical management and services accessed during an inpatient admission. A comparison of length of stay and inpatient mortality to age and gender matched control patients will also be undertaken.

2. To determine whether medical co-morbidities of patients with Parkinson's disease influence clinical management or health related outcomes during an inpatient admission.

3. To inform the cause of inpatient death, of patient's with Parkinson's disease as a primary and secondary diagnosis.

Hypothesis:

Patients with Parkinson's disease are likely to present with complaints characterised by their chronic neurological illness which are likely to directly influence their health related outcomes during an inpatient admission. Demographics, co-morbidities and management options are likely to differ between subdivided groups of PD patients as well as compared to controls. Patients with greater co-morbidities relating to their diagnosis of Parkinson's disease are likely to have a prolonged and complicated admission with a possible higher incidence of in hospital mortality. Uncharacterised co-morbidities not related to Parkinson's disease are likely to result in complicated inpatient management and increase the length of patient stay. The cause of PD inpatient death is likely to result from complicated co-morbidities relating to patient treatment. These causes of death are expected to differ compared to age matched controls.

Literature Summary:

Despite the manifest benefits to patients of early intervention and ongoing access to a range of specialised health services, there is a paucity of local New South Wales information relating to the reasons for PD patient hospital admissions, as well as patient associated co-morbidities. In 2009-10 there were 3179 hospitalisations for PD nationally. Although motor disturbances in PD are believed to be a significant cause for PD related admissions, other less defined causes are likely to influence hospitalisation, particularly non-motor complaints. Nationally it was estimated that in 2009-10, 2220 hospital admissions were recorded for accidental falls as well as 2138 admissions for pneumonia in the context of PD related complications. This was predicted to cost at least $76.6 million in addition to the health care system, as a result of PD related complications. Further, information regarding the types of health services that patients access as inpatients, along with the difficulty in tailoring focused neurological care are largely unknown within an Australian hospital setting.

Expected Benefits:

The findings of this study are expected to inform the development of recommendations to clinicians and support groups about optimising the pre-hospital care of patients with Parkinson's disease. Importantly this study's findings are expected to provide a well powered statistical analysis about the relevant reasons for admission that can guide resource allocation / funding within a local or state division. Further, publication of the common patient co-morbidities that lead to hospitalisation in PD may generate further awareness amongst clinicians and support the need for expanding activity based funding, based upon contemporaneous discharge summaries and admission documentation. Thirdly, the extended aim of investigating the cause of inpatient death for patients with a diagnosis of PD is believed to inform clinical governance in reviewing measures to prevent unexpected deaths as well as assisting in preparation for earlier end of life measures for the patient, family and clinicians. In addition it is believed that by providing direct feedback to Parkinson's Australia as well as other support groups, this study may offer many Australian sufferers with newly generated awareness to the importance of optimising outpatient PD management and improved chronic disease management through General Practice, avoiding unnecessary hospitalisations.

1.3 DESIGN OF THE STUDY

(a) What data collection technique(s) will be used? *[Type X to all that apply]*

Questionnaire(s)	
Interview(s)	
Observation of participant(s) with their knowledge	
Observation of participant(s) without their knowledge	
Audio- or video-taping interviewee(s) or event(s) with consent	
Other *[Provide details below in b]*	X

(b) Provide a description of the proposed research design and methodology and the anticipated outcomes.

[Refer to the National Statement Section 3 on Ethical considerations specific to research methods.]

Study design:

This study will comprise a retrospective cohort study of NSW Ministry of Health data.

Study sample:

New South Wales public and private hospital inpatient data; investigating reasons for admission based from the discharge diagnosis of Parkinson's disease, as a primary diagnosis and secondary diagnosis. Admission details are coded into disease-related groups (DRGs) using the International Classification of Disease (ICD). A consecutive five year period will be analysed from admission records from the NSW Ministry of Health. A representative age and gender matched control sample will also be obtained. Further linkage of inpatient death and their cause of death will be requested from the Australian Bureau of Statistics (ABS) at a later date.

Nil patient consent will be obtained. Data will be non-identifiable, with no patient names or addresses included.

Inclusion criteria:

Cases

Diagnosis of Parkinson's disease (Idiopathic Parkinson's disease) as either a primary or secondary diagnosis. (ICD-10-CM G20 coded)

Controls
Random data extraction of hospitalisations of any reason for admission during corresponding time intervals, representing 25% of cases. Age and gender matched sample to latest epidemiological prevalence data of PD in Australia. Gender ratio, 1.06:1 male to female respectively.

Exclusion criteria (Cases)

Other diagnosis of Parkinsonism, including atypical Parkinson's disease, secondary Parkinson's disease or Parkinson's Plus Syndromes.

1.4 USE OF INDEPENDENT CONTRACTORS

Will parts of this project be carried out by independent contractors?

(e.g. interviewing, questionnaire design, data analysis, sample testing)

X YES NO If YES, who is/are the independent contractor/s and describe what he/she will do in the context of this project.

[Ensure that any independent contractor/s will be engaged on the basis of relevant qualifications/experience and will receive a copy of the approved ethics protocol.]

Mr John Agland, is kindly assisting with extracting the project's requested data. (Manager, Performance Reporting. Health System Information and Performance Reporting Branch. NSW Ministry of Health).

The requested data is publically available and non-identifiable, however it is coded by DRG's. His department will decode our project's requested data from the NSW Ministry of Health database of hospital admissions.

1.5 RESEARCH LOCATION

(a) Will the research be undertaken on-site at The University of Notre Dame Australia?

X YES NO If No, give details of off-campus location.

UNDA - School of Medicine, Darlinghurst.

(b) Has permission to gain access to another location/organisation/institute been obtained?

YES X NO If Yes, specify from whom and attach a copy of the approval letter when available. If No, explain when the approval will be obtained.

No other site or location specific approvals have been made. No further HREC applications will be made.

1.6 MONITORING

[The Chief Investigator is responsible for providing annual and final progress reports to the HREC.]

(a) How will researchers monitor the conduct of the project to ensure that it complies with the protocol set out in this application, the University's Research Integrity Statement and the National Statement?

Ongoing surveillance throughout the duration of the project by all researchers that the project adheres to the original proposal guidelines. Nil changes or deviation to the original proposal will be made.

(b) How will the Chief Investigator monitor staff or students working interstate or overseas?

Not applicable.

1.7 INVOLVEMENT OF OTHER HREC(s)

(a) Has this project already been submitted to any other HREC(s)? YES X NO

(b) Will this project be submitted to any other HREC(s)? YES X NO

If you answered YES to (a) or (b), give the name of the HREC(s), and indicate the status of the application at each (i.e. submitted, approved, deferred or rejected). Attach copies of any correspondence. Indicate which committee you consider to be the primary HREC for this project and why.

2. PARTICIPANT DETAILS

[Refer to National Statement Section 4 on Ethical consideration specific to participants.]

2.1 TARGET PARTICIPANT GROUP

(a) Indicate the targeted participant group by typing X in the appropriate boxes.

[Expand any responses necessary in the space provided at "Other"]

Students or staff of this University		Adults (over 18 years old and competent to give consent)	
People from non-English speaking backgrounds		Children/legal minors (under 18 years old with parental consent) (* attach Appendix A to this application)	
Other *(Provide details below in b)*	X		

(b) Provide number, age range and source of participants.

Nil contact with patients / persons will be made during this study. Only existing coded data will be extracted which is non-identifiable and subsequently analysed.

(c) Where applicable, provide a justification of sample size, including details of statistical power of the sample, where appropriate, explaining how this sample size will achieve the objectives of the study.

[The quality and statistical validity of research is an essential condition of its ethical acceptability. Refer to the National Statement Chapter 1.1 on Research Merit and Integrity.]

Sample size calculation

A power calculation of a two population study, based on a probability Type 1 Error (α) of 0.05, Power (1-β) of 0.8 and expected proportions of group 1 of 0.01 and group 2 of 0.0025, indicated a required sample size of 1733 per group.

A large sample size is required to be reflective of a state wide analysis of Parkinson's disease admissions.

2.2 PARTICIPANT RECRUITMENT

(a) Indicate the method of recruitment by typing X in the appropriate boxes.

Mail out		Email	
Advertisement		Recruitment carried out by researcher/s	
Contact details obtained from public documents e.g phone book		Contact details obtained from private sources e.g employee list, membership database	
Participants from a previous study		Snowball (participants suggest other potential participants)	
Telephone			
Personal contacts			
Recruitment carried out by third party e.g employer, doctor			
Other *[Provide details in b) below]*	X		

(b) Provide details of recruitment strategies

(e.g. who will mail/telephone/approach participants, who will distribute a mail out, where an advertisement will be placed, third party, approval for contact details from private sources etc)

Not applicable to research.

2.3 DEPENDENT RELATIONSHIPS

[Refer to National Statement Chapter 4.3 on people in dependent or unequal relationships. A dependent or unequal relationship (eg. teacher/student, doctor/patient, student/lecturer, client/counselor) may compromise a participant's ability to give consent which is free from any form of direct or indirect threat or inducement.]

Are any of the participants in a dependent or unequal relationship with any of the researchers, particularly those involved in recruiting for or conducting the project?

YES X NO If Yes, explain the dependent or unequal relationship and the steps to be taken by the researchers to ensure that participation is purely voluntary and not adversely affected by the relationship).

2.4 PAYMENT OR INCENTIVES OFFERED TO PARTICIPANTS

[Refer to National Statement Sections 2.2.10 and 2.2.11 on reimbursing participants]

Do you propose to pay, reimburse or reward participants?

YES X NO If Yes, how, how much and for what purpose? Please justify the approach below.

3. INFORMATION FOR PARTICIPANTS AND INFORMED CONSENT

[Refer to Chapter 2.2 of the National Statement regarding general requirements for consent and 2.3 regarding qualifying or waiving conditions for consent. Information to participants must be provided at their level of comprehension regarding purpose, methods, demands, risks, inconveniences, discomforts and possible outcomes of the research. Information should be written in a Plain Language Statement. Each participant's consent must be clearly established by use of a signed Consent Form.]

3.1 PROVIDING INFORMATION FOR PARTICIPANTS

(a) Will you be providing participants with information in a written Plain Language Statement?

YES X NO If No, provide details of the protocol you will use to explain the research project to participants and invite their participation?

Not applicable to study

(b) Will arrangements be made to ensure that participants who have difficulty understanding English can comprehend the information provided about the research project?

YES X NO If Yes, what arrangements have been made? If No, give reasons.

Not applicable to study

3.2 PLAIN LANGUAGE STATEMENT NOT APPLICABLE X

(UNDA plain language statement templates can be found at http://www.nd.edu.au/research/hrec/apply.shtml)

CONFIRM THAT THE PLAIN LANGUAGE STATEMENT WILL *[type X to all that apply]*

- be printed on The University of Notre Dame Australia letterhead
- include clear identification of the School(s) involved, Project Title and Chief Investigator
- identification of other researchers and supervisors (including contact details), and the study level if it is a student research project
- provide details of the purpose of the research project
- provide details of what involvement in the project will require e.g. interview, questionnaire, audio- and/or video-taping of events, and estimated time commitment
- provide details of any risks involved and the procedures in place to minimise these
- state that the project has received ethical clearance by the HREC
- if the sample size is small, confirm that this may have implications for protecting the identity of the participants
- include a clear statement that if participants are in a dependent or unequal relationship with any of the researchers that involvement in the project will not affect ongoing assessment/grades/ management or treatment of health
- state that involvement in the project is voluntary and that participants are free to withdraw consent at any time, and to withdraw any unprocessed data previously supplied
- provide an explanation of arrangements for the protection of confidentiality of data, including that confidentiality of information provided is subject to legal limitations (see * below)
- provide advice as to whether or not data will be destroyed after a minimum period (if relevant)
- include the following statement : *If participants have any complaint regarding the manner in which a research project is conducted, it should be directed to the Executive Officer of the Human Research Ethics Committee, Research Office, The University of Notre Dame Australia, PO Box 1225 Fremantle WA 6959, phone (08) 9433 0943, research@nd.edu.au*

[– it is possible for data to be subject to subpoena, freedom of information request or legal reporting obligations. Depending on the research proposal you may need to specifically state these limitations on confidentiality]*

PLEASE ATTACH A COPY OF THE PLAIN LANGUAGE STATEMENT TO YOUR APPLICATION

3.3 OBTAINING CONSENT

(a) How will each participant's consent be established?

By signing and returning a Consent Form	By returning an anonymous survey
By a verbal agreement	By a recorded agreement for interview
By a person with lawful authority to consent (e.g. parent, doctor)	Other *(Please describe below):*

Not applicable to study

(b) If participants are unable to give informed consent, explain who will consent on their behalf and how such consent will be obtained and recorded.

Not applicable to study

3.4 CONSENT FORM

NOT APPLICABLE X

(Consent form templates can be found at http://www.nd.edu.au/research/hrec/apply.shtml)

CONFIRM THAT THE CONSENT FORM WILL *[type X to all that apply]*

1. be printed on The University of Notre Dame Australia letterhead
2. include the title of the project and names of researchers
3. state that the project is for research purposes
4. state that involvement in the project is voluntary, that participants are free to withdraw at any time and free to withdraw any unprocessed identifiable data previously supplied
5. outline particular requirements of participants (e.g whether interviews are to be audio and/or video-taped)
6. include arrangements to protect the confidentiality of data
7. include advice that there are legal limitations to data confidentiality (see * below)
8. if the sample size is small, confirm that this may have implications for protecting the identity of the participants
9. be retained by the researcher (once signed and returned)

[* – it is possible for data to be subject to subpoena, freedom of information request or legal reporting obligations. Depending on the research proposal you may need to specifically state and explain these limitations on confidentiality]

PLEASE ATTACH A COPY OF THE CONSENT FORM TO YOUR APPLICATION

4. PRIVACY AND CONFIDENTIALITY

[At the Commonwealth level, the collection, storage, use and disclosure of personal information by Commonwealth agencies is regulated by the Privacy Act 1988. There is regulation at State and Territory level in the form of legislation related to privacy generally or the administration of agencies, or administrative codes of practice.]

4.1 ANONYMITY/CONFIDENTIALITY OF PARTICIPANT IDENTITY *[type X to all that apply]*

Complete anonymity of participants X

(i.e. researchers will not know the identity of participants as participants return responses with no form of personal identification)

Non-identifiable samples or data X

(i.e. an irreversible process whereby identifiers are removed from data and replaced by a code, with no record retained of how the code relates to the identifiers. It is impossible to identify the individual to whom the information relates).

Re-identifiable samples or data

(i.e. a reversible process in which the identifiers are removed and replaced by a code. Those handling the data subsequently do so using the code. If necessary, it is possible to link the code to the original identifiers and identify the individual to whom the sample or information relates)

Participants have the option of being identified in any publication arising from the research

Participants will be referred to by pseudonym in any publication arising from the research.

Any other method of protecting the privacy of participants. [*Provide details below]*

Note that where the sample size is very small, it may be impossible to guarantee anonymity/confidentiality of participant identity. Participants involved in such projects need to be clearly advised of this limitation in the Plain Language Statement.

5. FEEDBACK AND OUTCOMES

5.1 How will the project outcomes be made public at the end of the project?

(e.g. thesis, journal article, book, web page, conference paper, the media etc).

Master's thesis submission to the UNDA School of Medicine, as well as the intent of publication in a peer reviewed international journal.

5.2 What feedback will be given to the participants and how will this feedback be given?

[Section 1.5 of the National Statement states 'research outcomes should be made accessible to research participants in a way that is timely and clear'.]

Not applicable to study

6. DATA STORAGE, SECURITY AND DISPOSAL

[Refer to Chapter 2 of the Australian Code for the Responsible Conduct of Research and University policy 'Code of Practice for name identified data' http://www.nd.edu.au/research/hrec/policies.shtml]

6.1 DATA STORAGE

Will data storage comply with the University policy?

X YES NO If No, please explain.

Data stored on campus at the University of Notre Dame, School of Medicine. Sydney.

6.2 DATA SECURITY

(a) Will only the listed researchers be responsible for the data collected and its security?

X YES NO If No, please provide further details. You may also use this space to explain any differences between arrangements in the field, and on return to campus.

(b) Which of the following methods will be used to ensure confidentiality of data? *[Type X to all that apply]*

- data and codes and all identifying information to be kept in separate locked filing cabinets X
- access to computer files to be available by password only X
- access by named researcher(s) only X
- other *(please describe below)*

6.3 DATA RETENTION AND DISPOSAL

[Refer to Chapter 2 of the Australian Code for the Responsible Conduct of Research. *Research data and records should be maintained for as long as they are of continuing value to the researcher and as long as recordkeeping requirements such as patent requirements, legislative and other regulatory requirements exist. This is usually five years after publication, or public release, of the work of the research and 15 years if the project involves clinical trial(s).]*

Specify how long materials (e.g. files, audiotapes, questionnaires, videotapes, photographs) collected during the study will be retained after the study and how they will ultimately be disposed of.

Five years post publication. Computer data will be deleted after this time period.

7. EXTERNAL FUNDING DETAILS (IF APPLICABLE)

7.1 Will the research be funded by a sponsor? (i.e. an individual, company or organisation that takes responsibility for initiation, management and financing of the research).

YES X NO (If YES, give details of source and amount of funding.)

Not applicable to study

7.2 (a) Will the research be funded by a granting body external to the university? (i.e. an organisation that provides research funding in the form of research grants or scholarships).

YES X NO

(b) What is the source of the External Funding?

ARC Scheme	Other Funding Source from within Australia
NHMRC Scheme	Other Funding Source from Overseas
US NIH Program	*(For "Other" please provide details* below)

Not applicable to study

(c) Please provide details of the external funding including registration number of grant/funding, proposed duration.

Not applicable to study

(d) Does the project require Human Ethics Approval before consideration for funding by granting body?

YES X NO *(If YES, what is the deadline for the granting body?)*

Not applicable to study

(e) How will participants be informed of the source of external funding?

Not applicable to study

8. CONFLICT OF INTEREST

[Refer to Chapter 5.4 regarding conflicts of interest.]

8.1 POTENTIAL CONFLICT OF INTEREST

Is there any affiliation or financial interest for researchers in this research or its outcomes or any circumstances which might represent a perceived, potential or actual conflict of interest?

YES X NO If Yes, give details below

University researchers must disclose and manage Conflict of Interest in accordance with the provisions of the university's 'Research Integrity Statement' http://www.nd.edu.au/downloads/research/research_integrity_aug06.pdf

In addition, if you have declared a potential conflict of interest, you are required to include an appropriate description of the potential conflict of interest on the Plain Language Statement and Consent Forms.

9. DECLARATION BY RESEARCHER(S)

The information contained herein is, to the best of my knowledge and belief, accurate.

I have read the *National Statement on Ethical Conduct in Human Research* (2007) and agree to comply with its provisions.

I have read the University's current human ethics guidelines, and accept responsibility for the conduct of the procedures set out in the attached application in accordance with the guidelines, the University's Code of conduct for Research and any other condition laid down by The University of Notre Dame Australia's Human Research Ethics Committee or School Research Committee.

I have attempted to identify all risks related to the research that may arise in conducting this research and acknowledge our obligations and the rights of the participants.

I have the appropriate qualifications, experience and facilities to conduct the research set out in the attached application and to deal with any emergencies and contingencies related to the research that may arise. If approval is granted, the project will be undertaken in strict accordance with the approved protocol and relevant laws, regulations and guidelines.

I/We agree:

- to commence this research project only after obtaining final approval from the Human Research Ethics Committee (HREC) sub-committee;
- to only carry out this research project where adequate funding is available to enable the project to be carried out according to good research practice and in an ethical manner;
- to provide additional information as requested by the SRC and/or HREC;
- to provide progress reports to the HREC including annual and final reports;
- to maintain the confidentiality of all data collected from or about project participants, and maintain security procedures for the protection of privacy;
- to immediately notify the SRC and HREC in writing if any change to the project is proposed and await approval before proceeding with the proposed change;
- to immediately notify the SRC and HREC in writing if any adverse event occurs after the approval by the SRC and/or HREC has been obtained;
- to agree to an audit if requested by the SRC and/or HREC;
- to only use data collected for the study for which approval has been given
- to notify the HREC if the project is discontinued prior to the expected date of completion;

All researchers listed on pages 1 and 2 must sign this declaration:

Researcher Name	Signature	Date

10. DECLARATION BY SCHOOL RESEARCH COMMITTEE [SRC]

DATE APPLICATION RECEIVED: / /

TECHNICAL REVIEW COMPLETED ETHICAL REVIEW COMPLETED

The SRC has reviewed this project and considers the methodological/technical and ethical aspects of the proposal to be appropriate to the tasks proposed.

YES NO

The SRC considers that the researcher has the necessary qualifications, experience and facilities to conduct the research set out in the attached application, and will be able to deal with any emergencies and contingencies that may arise.

YES NO

Please provide a short report detailing the outcomes of the SRC review of this application, including any important details of the application, the decision and reasons for the decision.

Name of SRC Chair	
Signature	
Date	

Note: If the SRC Chair is also named as a Researcher for this project, the declaration cannot be signed by that person and must be signed by another authorised member of the SRC.

Once reviewed, the SRC must forward the original application, including the checklist and all attachments, to the Executive Officer of the HREC for review by the HREC sub-committee.

11. LOW RISK REVIEW CHECKLIST AND OTHER ATTACHMENTS

Please check that the following documents are attached to your application.

11.1 LOW RISK REVIEW CHECKLIST

Have you completed and attached to your application the Low Risk Review Checklist?

[Note: Low Risk Review cannot take place without this checklist being attached to the application]

YES X NO

11.2 OTHER ATTACHMENTS

(Please note that where questionnaire or interview questions are submitted in draft form, a copy of the final documentation must be submitted for final approval when available)

Document	Yes	Draft Only	Final Version	N/A
Reference list (Section 1.2)				X
Questionnaire and/or List of interview questions (section 1.3)				X
Evidence of external approvals related to the research (Section 1.5)				X
Approvals/Correspondence with other HREC(s) (Section 1.7)				X
Research Involving Children Form – Appendix A (Section 2.1)				X
Recruitment advertisement, approvals (Section 2.2)				X
Plain Language Statement (PLS) (Section 3.2)				X
Consent Form (Section 3.4)				X

APPENDIX 2 – COVER LETTER TO JOURNAL EDITOR

SUBJECT: Submission of new manuscript for evaluation

03.02.2014

Dear Professor Kiernan,

I enclose a manuscript entitled **"Hospitalisation and comorbidities in Parkinson's disease: a large Australian retrospective study"** for your consideration.

This manuscript has not been published elsewhere, accepted for publication elsewhere or under editorial review for publication elsewhere. All authors have read the final manuscript, as have representatives of The University of Notre Dame Australia. There was no ghost writing by anyone not named on the author list. This manuscript reports the results of an original research project conducted from 01.01.2013 to 31.01.2014. Ethics committee approval was secured for the study from the University of Notre Dame, HREC.

The research project was conducted under the guidance of: Associate Professor R. Louise Rushworth (Medical Epidemiologist) and Dr Stephen Tisch (Movement Disorder specialist, Neurology consultant) at St Vincent's Hospital, Darlinghurst Sydney. All three authors have previously published original work relating to Parkinson's disease and clinical epidemiology in peer reviewed international journals. We believe that the entirety of our manuscript would benefit from publication in the print version of the article rather than in web only files, so as not to detract from the consistency of our reporting.

A brief overview of the significant results of the manuscript are:

- The study identified important patterns of hospitalisation from a large group of Parkinson's disease patients within Australia. Demographic and clinical features were able to be compared to an age and gender matched control sample of patients within NSW.
- Common causes for hospitalisation were identified as well as recommendations made to improve patient care during hospital admissions.

- Parkinson's disease patients were identified as having significantly longer hospital stays than control patients, as well as being more likely to be treated for delirium, adverse drug events, syncope, falls / fractures, dementia, gastrointestinal complications, genitourinary infections, reduced mobility and other trauma but less likely to require hospitalisation for chronic airways disease and neoplasia, including melanoma than control patients.
- Procedures including Deep Brain Stimulation were analysed, showing selective use by particular candidates during hospitalisation.

We believe that publication of the results of this project in the Journal of Neurology, Neurosurgery, and Psychiatry will inform the clinical practice of treating specialist clinicians as well as epidemiologists and researchers, and assist in improving the health outcomes of patients with Parkinson's disease.

Word count: 3337 Abstract word count: 247

Yours sincerely,

Dr Michal Lubomski (lead author)

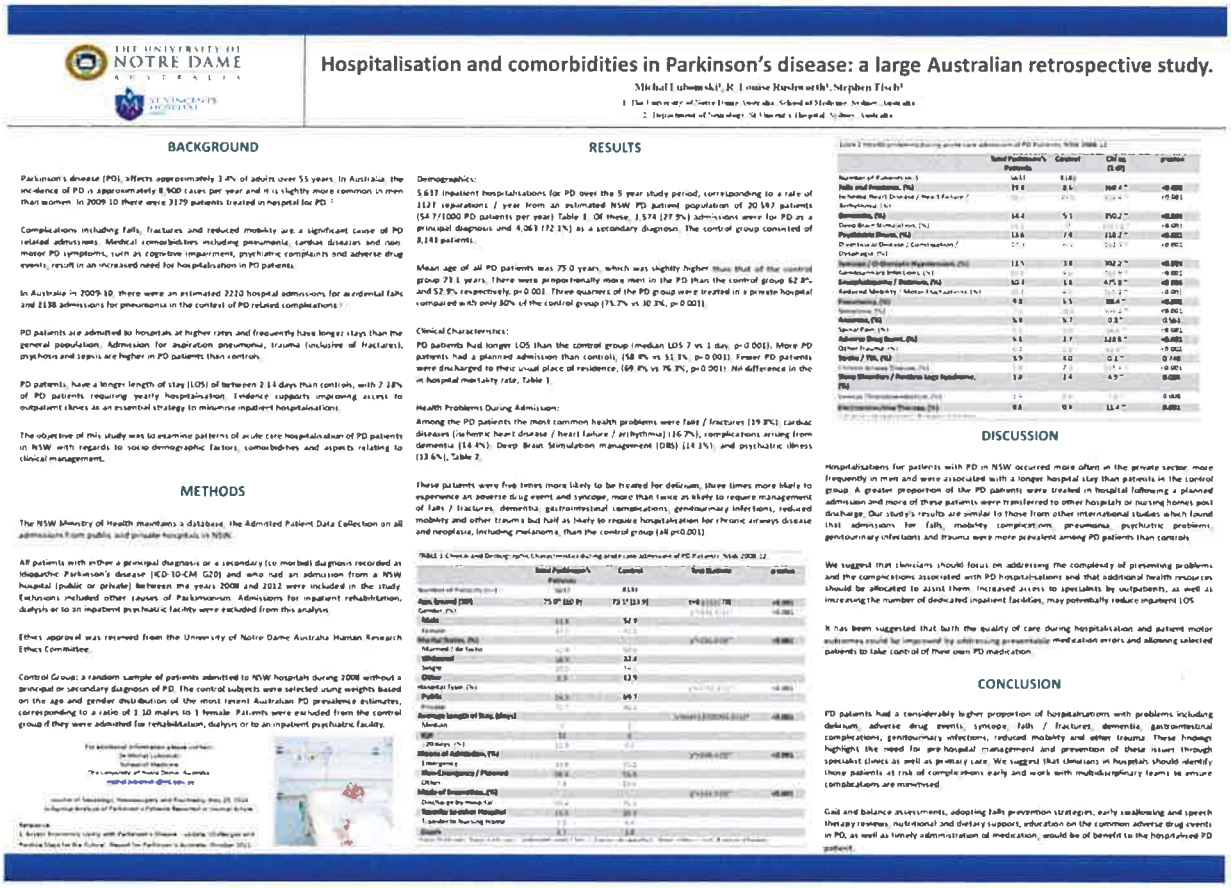
For Associate Professor Louise Rushworth and Dr Stephen Tisch.

APPENDIX 3 – MDSA CONFERENCE

Movement Disorder Society of Australia – Conference. Queenstown, New Zealand : August 18-19th – 2014.

Poster presentation:

- **Copy of actual poster that was presented.**



THE UNIVERSITY OF NOTRE DAME AUSTRALIA

Hospitalisation and comorbidities in Parkinson's disease: a large Australian retrospective study.

Michal Lubomski[1], K Louise Rawlinson[1], Stephen Finch[2]

1 The University of Notre Dame Australia, School of Medicine, Sydney, NSW, Australia
2 Department of Neurology, St Vincent's Hospital, Sydney, NSW, Australia

BACKGROUND

Parkinson's disease (PD), affects approximately 1.4% of adults over 55 years. In Australia, the incidence of PD is approximately 8,900 cases per year and it is slightly more common in men than women. In 2009-10 there were 3179 patients treated in hospital for PD.

Complications including falls, fractures and reduced mobility are a significant cause of PD related admissions. Medical complications including pneumonia, cardiac disease and non motor PD symptoms, such as cognitive impairment, psychiatric complaints and adverse drug events, result in an increased need for hospitalisation in PD patients.

In Australia in 2009-10, there were an estimated 2210 hospital admissions for accidental falls and 2138 admissions for pneumonia in the context of PD related complications.

PD patients are admitted to hospitals at higher rates and frequently have longer stays than the general population. Admission for aspiration pneumonia, trauma (inclusive of fractures), psychosis and sepsis are higher in PD patients than controls.

PD patients, have a longer length of stay (LOS) of between 2.14 days than controls, with 7.28% of PD patients requiring yearly hospitalisation. Evidence supports improving access to outpatient clinics as an essential strategy to minimise inpatient hospitalisations.

The objective of this study was to examine patterns of acute care hospitalisation of PD patients in NSW with regards to socio demographic factors, comorbidities and aspects relating to clinical management.

METHODS

The NSW Ministry of Health maintains a database, the Admitted Patient Data Collection on all admissions from public and private hospitals in NSW.

All patients with either a principal diagnosis or a secondary (co morbid) diagnosis recorded as Idiopathic Parkinson's disease (ICD-10-CM G20) and who had an admission from a NSW hospital (public or private) between the years 2008 and 2012 were included in the study. Exclusions included other causes of Parkinsonism. Admissions for inpatient rehabilitation, dialysis or to an inpatient psychiatric facility were excluded from this analysis.

Ethics approval was received from the University of Notre Dame Australia Human Research Ethics Committee.

Control Group: a random sample of patients admitted to NSW hospitals during 2008 without a principal or secondary diagnosis of PD. The control subjects were selected using weights based on the age and gender distribution of the most recent Australian PD prevalence estimates, corresponding to a ratio of 1.10 males to 1 female. Patients were excluded from the control group if they were admitted for rehabilitation, dialysis or to an inpatient psychiatric facility.

RESULTS

Demographics:

5 617 inpatient hospitalisations for PD over the 5 year study period, corresponding to a rate of 1127 separations / year from an estimated NSW PD patient population of 20 587 patients (54.7/1000 PD patients per year) Table 1. Of these, 1 574 (27.9%) admissions were for PD as a principal diagnosis and 4,063 (72.1%) as a secondary diagnosis. The control group consisted of 8,181 patients.

Mean age of all PD patients was 75.0 years, which was slightly higher than that of the control group 73.1 years. There were proportionally more men in the PD than the control group 62.8% and 52.9% respectively, p<0.001. Three quarters of the PD group were treated in a private hospital compared with only 30% of the control group (75.7% vs 30.3%, p<0.001).

Clinical Characteristics:

PD patients had longer LOS than the control group (median LOS 7 vs 1 day, p<0.001). More PD patients had a planned admission than controls, (58.8% vs 51.3%, p<0.001). Fewer PD patients were discharged to their usual place of residence, (69.8% vs 76.3%, p<0.001). No difference in the in hospital mortality rate, Table 1.

Health Problems During Admission:

Among the PD patients the most common health problems were falls / fractures (19.8%); cardiac diseases (ischemic heart disease / heart failure / arrhythmia) (16.7%), complications arising from dementia (14.4%); Deep Brain Stimulation management (DBS) (14.3%); and psychiatric illness (13.6%), Table 2.

These patients were five times more likely to be treated for delirium, three times more likely to experience an adverse drug event and syncope, more than twice as likely to require management of falls / fractures, dementia, gastrointestinal complications, genitourinary infections, reduced mobility and other trauma but half as likely to require hospitalisation for chronic airways disease and neoplasia, including melanoma, than the control group (all p<0.001).

DISCUSSION

Hospitalisations for patients with PD in NSW occurred more often in the private sector, more frequently in men and were associated with a longer hospital stay than patients in the control group. A greater proportion of the PD patients were treated in hospital following a planned admission and more of these patients were transferred to other hospitals or nursing homes post discharge. Our study's results are similar to those from other international studies which found that admissions for falls, mobility complications, pneumonia, psychiatric problems, genitourinary infections and trauma were more prevalent among PD patients than controls.

We suggest that clinicians should focus on addressing the complexity of presenting problems and the complications associated with PD hospitalisations and that additional health resources should be allocated to assist them. Increased access to specialists by outpatients, as well as increasing the number of dedicated inpatient facilities, may potentially reduce inpatient LOS.

It has been suggested that both the quality of care during hospitalisation and patient motor outcomes could be improved by addressing preventable medication errors and allowing selected patients to take control of their own PD medication.

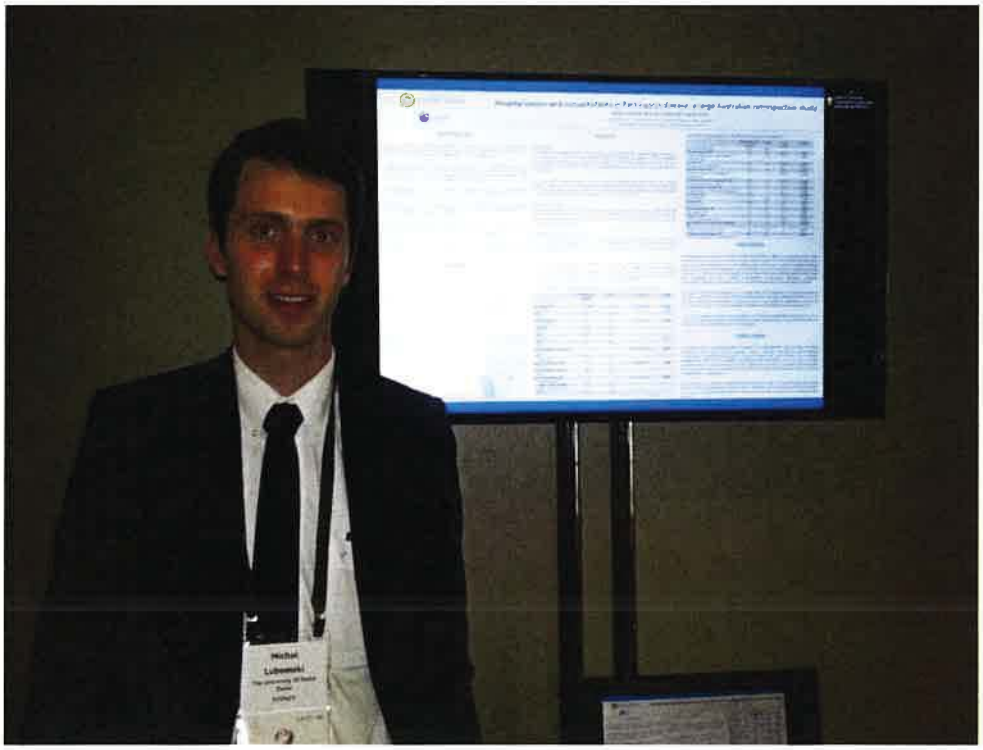
CONCLUSION

PD patients had a considerably higher proportion of hospitalisations with problems including delirium, adverse drug events, syncope, falls / fractures, dementia, gastrointestinal complications, genitourinary infections, reduced mobility and other trauma. These findings highlight the need for pre-hospital management and prevention of these issues through specialist clinics as well as primary care. We suggest that clinicians in hospitals should identify those patients at risk of complications early and work with multidisciplinary teams to ensure complications are minimised.

Gait and balance assessments, adopting falls prevention strategies, early swallowing and speech therapy reviews, nutritional and dietary support, education on the common adverse drug events in PD, as well as timely administration of medication, would be of benefit to the hospitalised PD patient.

Awarded 1st Prize for Poster Presentations.

Photographs of Michal Lubomski at the poster presentation. (August 18th 2014)



APPENDIX 4 – NEWS REPORT

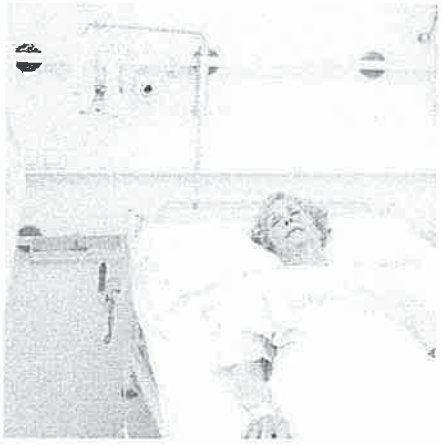
News Article Publication – Neurology Update. June 2014.

A weekly newsletter for Australian neurologists and related professionals.

Attached is a copy of the electronic publication.

More resources needed for Parkinson's admissions: experts

4 June, 2014 Hugo Wilcken 0 comments Read Later



Patients with Parkinson's disease admitted for acute care are far more likely to suffer serious complications compared with other acute care patients, **new Australian research** finds.

The study of all patients with idiopathic Parkinson's disease (PD) admitted in NSW between 2008 and 2012 showed they were five times more likely to be treated for delirium and three times more likely to experience an adverse drug event and syncope compared with acute care controls.

They were more than twice as likely to require management for falls and fractures, dementia, gastrointestinal complications, genitourinary infections, reduced mobility and other trauma, the researchers from Sydney's University of Notre Dame and St Vincent's hospital found.

However they were only half as likely to need hospitalisation for chronic airways disease or neoplasia including melanoma, the authors said, even though previous research had postulated a link between levodopa use and melanoma.

The findings "highlight PD as a multisystem neuropsychiatric disorder in which motor and non-motor features contribute to morbidity," the authors wrote in the *Journal of Neurology, Neurosurgery and Psychiatry*.

Clinicians should focus on addressing the complexity of presenting problems and "additional health resources should be allocated to assist them," they said.

Outpatients should have better access to specialists and the number of dedicated inpatient facilities, similar to stroke units, needed to be increased, they added.

Patient outcomes could also be improved by addressing preventable medication errors and allowing some patients to take control of their own PD medication, they suggested.

This was because non-neurology admitting teams were not as familiar with the time criticality of PD medications, particularly in patients with motor fluctuations, they said.

"We suggest that clinicians in hospitals should identify those patients at risk of complications early and work with multidisciplinary teams to ensure complications are minimised."

***Journal of Neurology, Neurosurgery and Psychiatry* 2014; online**

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Large study confirms thrombectomy efficacy

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PeterR
Thats just the figure given in the UK's NHS material. I saw a study saying 3 months too but I don't know if that included longer term...
Antivax film dummped following outcry · 3 hours ago

Rodney Barkman
Historically, patients with renal colic were sent horse-riding, bare-back!
A novel way treat kidney stones · 4 hours ago

Dr Phil 42
References??? I thought it faded out from as early as 3 months
Antivax film dummped following outcry · 7 hours ago

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