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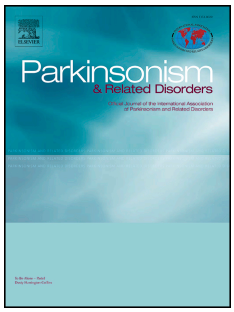

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A systematic review of interventions to reduce hospitalisation in Parkinson's disease

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Key words: Parkinson's disease, hospitalisation, interventions, randomised controlled trial

Abstract

The neurodegenerative process in Parkinson's disease (PD) results in a relentless progression of motor and non-motor symptoms. Affected individuals are frequently hospitalised for complications of the disease including falls, fractures, infections, and neuropsychiatric symptoms. When admitted to hospital, inpatient care is often suboptimal as it focusses on the primary cause of admission, and is associated with poor patient outcomes and significant healthcare costs. **Aim**: To review existing literature for evidence-based interventions aimed at reducing hospital admissions in PD **Methods:** Electronic literature search in EMBASE, MEDLINE and CINAHL databases for studies evaluating interventions to reduce hospital admissions in PD. We included publications with full abstracts, published in the English language and addressing interventions to reduce hospital admissions in PD. **Results:** To date there are no randomised controlled trials addressing the topic. We identified nine relevant retrospective studies. Results from these studies suggest an association between frequent neurologist consultations, open access clinics, and medication compliance with a reduction in PD hospital admissions and emergency room visits. **Conclusion:** This systematic review highlights the lack of robust evidence for measures aimed at reducing hospital admissions in people with PD. Future prospective studies are required to evaluate the effectiveness of proposed interventions.

Word count: 2668

Introduction

Motor and non-motor symptoms in Parkinson's disease (PD) steadily progress with advancing disease leading to complications such as falls, fractures, and infections; which are compounded by cognitive decline and Parkinson's dementia. As a consequence, individuals with the disease are admitted to hospital more often than people without PD.[1, 2] In addition, medication-related complications add to the disease burden and increase the likelihood of hospital encounters.[3] Once PD patients are admitted to hospital, they have prolonged inpatient stays,[4] poor motor outcomes, infections, prescription errors, increased postoperative mortality,[5-8] and are more likely to have repeat hospital admissions.[9] A study in the United States reported a significant economic burden from PD hospitalisation: approximately 20% of estimated annual cost for PD ($4.6 billion US dollars) was due to inpatient costs.[4] Similarly in the UK, there is a substantial cost from non-elective PD admissions (annual expenditure £194 million).[10] Given the aging population, these costs are likely to rise.

Given the scale of PD hospitalisation, the associated morbidity, mortality, and costs, there is a need for interventions to reduce unplanned PD hospital admission. Such interventions should be cost-effective and focussed on reducing known risk factors for hospitalisation. The purpose of this article was to systematically review available literature for effective interventions aimed at preventing unplanned hospital admissions in individuals with PD.

Methods

A search for publications from EMBASE, MEDLINE and CINAHL databases up to September 2014 was performed. Eligibility criteria included randomised controlled trials

(RCTs) evaluating effectiveness of intervention versus no intervention in reducing hospital admissions and/or emergency department visits in patients with PD. Index terms and free text terms for 'Parkinson's disease', Parkinson*, 'hospitalisation', and hospital* were used but this yielded no relevant randomised controlled trials. The search criteria were therefore broadened to include other study types. We included all studies where a specific measure was employed and led to a reduction in number of hospital admissions or emergency department visits in PD. Interventions included those that have been used in other chronic diseases to reduce unplanned hospital admissions such as patient educational programmes, urgent access clinics, specialist's clinics and specialist nurses. Outcome measures included a reduction in either hospital admission, non-elective, unplanned admissions, or emergency room visits. Study participants were individuals with PD of all disease stages and duration. No age restrictions were applied. Abstracts and title headings were screened and only publications with full abstracts, published in the English language and addressing interventions to reduce hospital admissions in PD were included.

Results.

7,610 abstracts obtained from the three data sources were screened. Duplicates and publications addressing hospitalisation in conditions other than PD were excluded. 115 articles and abstracts were assessed for eligibility. From these, 105 excluded articles discussed issues pertaining to PD hospitalisation such as frequency and reasons for admissions, inpatient care and medication errors, but did not assess the effect of specific interventions on reducing hospital admissions in PD (figure 1). We found one randomised controlled trial (RCT) which assessed the effectiveness of two dysphagia management techniques in reducing the aspiration pneumonia and also measured hospitalisations as an adverse event.[11] Nine retrospective studies reported a change in healthcare utilisation

including the number of emergency visits and or hospitalisation after an intervention and these were included (Table 1). [12-20]

One RCT compared the incidence of pneumonia among 515 patients with dementia and PD who were randomised to either chin-down posture technique or two types of thickened fluids (nectar- and honey-thick consistencies) over a 3 month follow up period.[11] There was no difference in the incidence of pneumonia (primary outcome measure) between the two interventions. When the two types of thickened fluids were compared the cumulative incidence for pneumonia was less in the nectar-thick fluid compared to honey-thick fluid (0.08 and 0.15 respectively; HR 0.50 95% CI 0.23, 1.09).[11] The overall incidence of pneumonia reported in this study was low, however authors could not attribute the low incidence to the interventions used in this study because no placebo group was included.[11] Hospitalisations were reported as an adverse event and 20% of participants had at least one hospital admission in each of the two intervention arms. The number of withdrawals due to adverse events, including hospitalisations, was higher in the thickened fluid group (4%) compared to chin down posture group (2%); 2% difference, CI -0.4%, -5%).

A retrospective cohort study among 24,929 Medicare recipients in the United States (US) evaluated the effect of frequent neurologist care on PD hospitalisation and reported a reduction in hospital admissions for traumatic injury (HR 0.56, 95% CI 0.40-0.78), psychosis (HR 0.71, 95% CI 0.59-0.86) and urinary tract infection (HR 0.74 95% CI 0.63-0.87) in patients who had frequent neurologist care compared to those who were not treated by a neurologist.[12] Another US survey assessed the impact of neurologist care on healthcare costs and utilisation among 3,883 individuals with chronic neurological conditions including parkinsonism and showed that respondents who had consulted a neurologist had a reduction in disease-related home care, emergency, and inpatient care events compared to those with no neurologist involvement (OR 0.64, P=0.001).[13] In another retrospective study, PD patients

with poor motor symptom control, medication-related complications, or neuropsychiatric symptoms were allowed to access an urgent neurology clinic without prior appointment. This resulted in a 50% reduction in PD admissions over a 2 year period.[14] In addition there was a reduction in hospital length of stay from 11 to 4.5 days.[14]

Two retrospective studies reported fewer hospital admissions in PD patients treated with rasagiline when compared to dopamine agonists[15] or selegiline.[16] Comparisons of the number, duration, and cost of hospital admissions for 7,230 PD patients who were initially treated with either a dopamine agonist or rasagiline were compared using data from the Medicare Supplemental Database. The authors reported fewer hospital admissions (OR 0.76, 95% CI 0.66-0.86), shorter duration of stay (-0.38 day $p< 0.0001$), and reduced costs in rasagiline-treated patients compared to the DA group: $12,327 versus $16,525 respectively.[15] In a retrospective study involving 3,864 individuals with PD, Grubb *et al* showed that, rasagiline use was associated with lower emergency room visits (odds ratio: 0.79; 95% CI, 0.68 to 0.92) and all cause hospital admissions (odds ratio: 0.82; 95% CI, 0.68 to 0.99) compared to the selegiline-treated group.[16] However, no difference was found in the odds of PD-related hospital admissions and fractures.[16]

Four retrospective studies assessed the frequency of medication adherence in PD and also measured hospitalisation as an outcome. In a retrospective historical cohort study which included 1,215 from a US health claim database, Delea *et al* showed that patients with satisfactory levodopa/carbidopa/entacapone therapy compliance (proportion of days where a patient had medication supply $\geq$80%), had 49% fewer emergency room visits ($p=0.010$) and 39% less PD-related hospitalisations compared to the non-adherent group ($p=0.001$).[17] The number of all hospitalisations and overall PD-related costs were also lower in the group of patients with satisfactory treatment adherence.[17] In another study of 104 PD patients, suboptimal adherence to PD medication was associated with worsening motor symptoms.[19]

PD related hospitalisations and emergency room visits were used as an indicator of worsening motor symptoms, in addition to an increase PD medication dosage. Medication possession ratio (MPR), a measure of medication adherence was defined as the proportion of days covered by a PD prescription: the numerator was the number of days covered by a PD prescription and the denominator was the number of days between prescription disbursements.[19]. During the first year of follow up, the mean possession ratio, PD related emergency room visits, and hospitalisation were 0.52 ± 0.35, 0.07 ± 0.29, and 0.91± 2.19 respectively. In the 5th year the MPR was lower 0.42 ± 0.37 with higher emergency room visits and hospitalisation: 0.18± 0.70 and 1.40± 3.74. [19] In a retrospective cross-sectional study, Wei *et al* used Medicare administrative data for 7,583 patients with PD and found that those with a medication possession ratio of more than 90% had lower emergency room visits and hospitalisation rate than poor adherers (less 80% MPR).[18] Another US study evaluated the prevalence and cost of poor adherence to PD medication using retrospective administrative and claims data. The study included 3,119 participants who had a PD International classification of diseases (ICD) code recorded and were on PD medications during the study period. The mean number of hospitalisations over 12 months was significantly higher amongst individuals who were non-compliant with PD medication in comparison to the compliant group (2.3 versus 1.8; $p<0.005$).[20] However, there was no difference in the mean number of emergency room visits.[20] Mean health costs were significantly higher in the non-adherent group.[20]

Discussion

Hospitalisation in PD is a significant cost-driver[21] and patient outcome is often poor.[3-5] This review highlights the lack of evidence-based interventions for reducing PD patient hospitalisation.

Of the few studies we did find in this area, only one RCT of a specific intervention was found. This reported an low overall pneumonia incidence and no difference in the frequency of pneumonia when either chin-down posture or thickened fluids were used to manage dysphagia.[11] This study was limited by a short follow up period and the absence of a control group.[11] There was no difference in hospitalisation rates between the two interventions. Further, the cumulative pneumonia incidence was less when fluids with nectar compared to honey consistency were used.[11] This difference could have been a chance finding because the overall incidence of pneumonia in the study was low. Although speculative, the low pneumonia rates reported in the study suggests that chin-down posture and fluids of nectar/honey consistency may be useful interventions for pneumonia prevention.

We identified nine retrospective studies where hospitalisation rates and emergency room visits in PD were measured. These studies suggested that frequent neurologist consultation, open access clinics, and compliance with PD medication may reduce hospital admissions and emergency room attendance by PD patients. The cost effectiveness and the actual number and frequency of neurological consultations required to reduce PD hospitalisation is uncertain. Frequent consultations may provide opportunities for medication adjustments, earlier detection and management of complications which, in turn, reduces the need for hospitalisation.[12] Open access clinics also provide similar opportunities for symptoms and complication management which potentially prevents hospital admissions.[14] The effectiveness of open access clinics was based on a report from a single centre with no comparison group. An association between PD medication adherence and reduction in emergency room visits and PD-related hospital admissions was reported in four retrospective studies.[17-20] Sub-optimal adherence to PD medication can have negative implications on motor outcomes and patient quality of life.[22] These findings imply that optimising PD symptom control through medication compliance possibly reduces hospital admissions for

poor motor control. Interventions such as regular neurologist care and open access clinics may be difficult to implement in countries where some individuals have no health insurance. In addition, some patients may not be able to afford their PD prescriptions which may impact on medication adherence, motor symptom control, and therefore hospitalisation. A surprising finding was the association between rasagiline treatment and fewer hospital admissions reported in two retrospective studies.[15, 16] Dopamine agonists have superior symptomatic effects compared to monoamine oxidase inhibitor treatment. However, dopamine agonist treatment is associated with more side effects.[23] This may account for the fewer hospitalisations in rasagiline group. The differences in emergency room visits between selegiline and rasagiline treated patients cannot be explained. These two studies were funded by the rasagiline manufacturer which may have led to bias.

A major limitation of these studies is their retrospective design. Reliability of the reported results is dependent on the accuracy of the databases from which the data were extracted. It is also impossible to control for all confounding factors in such studies. Therefore, definitive conclusions regarding the effectiveness of the above interventions cannot be drawn based on this evidence. Nevertheless, these studies provide some insight into the interventions that require further evaluation.

Falls, fractures, infections, cognitive, and motor decline have been identified as risk factors for unplanned hospital admissions in patients with PD.[9] Implementing preventative measures for these complications may reduce the need for hospital admission. Falls in PD can occur as a result of postural instability, poor motor symptom control, and drug-related side effects (e.g. postural hypotension). Optimising motor symptom control and managing medication side effects may prevent falls and hence hospital admissions. Furthermore physiotherapy is thought to improve PD motor symptoms, mobility, and balance,[24] which may also potentially reduce the risk of falls. A recent Cochrane review compared the

effectiveness of physiotherapy interventions and no intervention in PD on outcomes such as gait, falls, and clinician-rated measures of impairment and disability. Health resource usage including hospitalisation was not reported as an outcome measure. Although there was a reported trend towards improvement in falls, there was no significant difference in the number of falls between the physiotherapy and non-intervention arms in 6 studies from which data could be abstracted.[24] The authors reported that the absence of a positive effect from physiotherapy could have been a result of short follow up periods, reliance on falls diaries, and the small number of participants in the included studies.[24] In terms of fracture prevention, there is good evidence that osteoporosis prevention strategies such as Vitamin D supplementation and bisphosphonates improve bone mineral density and reduce fracture risk in PD.[25] Fracture prevention measures may reduce hospitalisation as shown in an Italian retrospective study which included 5,167 postmenopausal women who were discharged from hospital with primary or secondary diagnosis of hip fracture.[26] The study compared the effect of treatment or no treatment with fracture prevention medication on mortality, re-fracture rates, and costs of health resource use (including hospitalisation). For those who were treated with bisphosphonates, the effect of compliance with treatment on these outcome measures was also assessed.[26] Only 34% of the included patients were exposed to fracture prevention treatments and 1,044 events (deaths and hospitalisation) were reported, and these were related to re-fractures.[26] A significantly reduced incidence of death (-55%, $p<0.001$) and re-fracture related hospitalisations (-40% $p<0.001$) was reported when fracture treatment was used.[26] In those who were treated with bisphosphonates, adherence of <40% was associated with higher total costs including re-hospitalisation, compared to those with better adherence.[26] It is uncertain if osteoporosis and fracture prevention measures translate into a reduction in hospitalisation rates in PD. Early speech and language therapy involvement in dysphagia management may potentially reduce the number of hospital admissions for

aspiration pneumonia. To date, no studies have systematically assessed whether pneumonia, falls, and fracture prevention strategies discussed above can reduce the number of hospital admissions in PD.

PD nurse specialists, where available, may play a crucial role in identifying PD patients in the community who are at high risk of hospitalisation. By working in liaison with other PD specialists in primary and secondary care, social services, palliative care and rehabilitation services, early treatment can be instituted in the patients' home. Community PD nurse care has been shown to be cost neutral when compared to primary care physicians, in a randomised controlled trial.[27] However, effectiveness of this approach in reducing PD hospitalisation rates has not been assessed.

Interventions such as specialist clinics (multidisciplinary or nurse-led),[28] medication management,[29] and patient self-management educational programmes,[30] have been shown to be effective in reducing unplanned admissions in other chronic conditions. The limited evidence that is available in PD does suggest that specialist clinics and medication management may reduce hospitalisation and therefore these interventions require further evaluation.

This systematic review has highlighted a gap in evidence-base for interventions that are effective in reducing PD hospital admissions. Proposed measures are based mainly on retrospective studies and none have been systematically assessed in PD. Nevertheless, these interventions merit further evaluation in well-designed prospective trials. Considering the complexity of managing PD, it is likely that a multimodal approach which addresses motor and non-motor complications, as well as palliatives aspects in end-stage disease, may be more effective compared to a single intervention approach. In view of the health costs and morbidity associated with PD hospitalisation, it is imperative that PD experts and policy

makers make a joint effort to finding ways to reduce hospitalisation in PD as the search for disease modifying treatment continues.

Author contributions

Sharon Muzerengi: Review of literature and first manuscript draft.

Clare Herd: Search strategy, reviewed literature and comments on manuscript.

Caroline Rick: reviewed and commented on manuscript.

Carl E Clarke: Project conception, reviewed and commented on manuscript

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References

[1] Guttman M, Slaughter P.M, Theriault M.E, DeBoer D.P, Naylor C.D. Burden of Parkinsonism a population based study. Mov Disord. 2003;18:313-9.

[2] Hobson DE, Lix LM, Azimaee M, Leslie WD, Burchill C, Hobson S. Healthcare utilization in patients with Parkinson's disease: a population-based analysis. Parkinsonism & related disorders. 2012;18:930-5.

[3] Temlett JA, Thompson PD. Reasons for admission to hospital for Parkinson's disease. Internal medicine journal. 2006;36:524-6.

[4] Huse D, Schulman K, Orsini L, Castelli-Haley J, Kennedy S, Lenhart G. Burden of illness in Parkinson's disease. Movement disorders : official journal of the Movement Disorder Society. 2005;20:1449-54.

[5] Mueller MC, Juptner U, Wuellner U, Wirz S, Turler A, Hirner A, et al. Parkinson's disease influences the perioperative risk profile in surgery. Langenbeck's archives of surgery / Deutsche Gesellschaft fur Chirurgie. 2009;394:511-5.

[6] Gerlach OH, Broen MP, van Domburg PH, Vermeij AJ, Weber WE. Deterioration of Parkinson's disease during hospitalization: survey of 684 patients. BMC neurology. 2012;12:13.

[7] Gerlach OH, Broen MP, Weber WE. Motor outcomes during hospitalization in Parkinson's disease patients: a prospective study. Parkinsonism & related disorders. 2013;19:737-41.

[8] Harris-Hayes M, Willis AW, Klein SE, Czuppon S, Crowner B, Racette BA. Relative mortality in U.S. Medicare beneficiaries with Parkinson disease and hip and pelvic fractures. The Journal of bone and joint surgery American volume. 2014;96:e27.

[9] Hassan A, Wu S, Schmidt P, Dai Y, Simuni T, Giladi N, et al. High rates and the risk factors for emergency room visits and hospitalization in Parkinson's disease. Parkinsonism & related disorders. 2013;19:949-54.

[10] Low V, Ben-Shlomo Y, Coward E, Fletcher S, Walker R, Clarke CE. Measuring the burden and mortality of hospitalisation in Parkinson's disease: A cross-sectional analysis of the English Hospital Episodes Statistics database 2009-2013. Parkinsonism & related disorders. 2015;21:449-54.

[11] Robbins J. GG, Hind J., Logemann J.A., Lindblad A.S., Brandt D., Baum H., Lilienfeld D., Kosek S., Lundy D., Dikeman K., Kazandjian M., Gramigna G.D., McGarvey-Toler S., Miller Gardner P.J. . Comparison of 2 interventions for liquid aspiration on pneumonia incidence A randomized trial. Annals of Internal Medicine. 2008;148:509-18.

[12] Willis AW, Schootman M, Tran R, Kung N, Evanoff BA, Perlmutter JS, et al. Neurologist-associated reduction in PD-related hospitalizations and health care expenditures. Neurology. 2012;79:1774-80.

[13] Ney J, Van Der Goes D. Effect of neurologist ambulatory visits on utilization and expenditures of non-ambulatory care in the united states. Neurology. 2013;80 (1 MeetingAbstracts).

[14] Klein C, Prokhorov T, Miniovitz A, Dobronevsky E, Rabey JM. Admission of Parkinsonian patients to a neurological ward in a community hospital. Journal of Neural Transmission. 2009;116:1509-12.

[15] Grubb E, Jackson J, Lage M.J, Treglia M. Comparison of hospitalizations among Parkinson's patients who initiated therapy with a dopamine agonist or rasagiline Evidence from the medicare supplemental database. Value in Health Conference: ISPOR 15th Annual European Congress Berlin Germany Conference. 2012;15:A558.

[16] Grubb E, Treglia M, Lage M, Castelli-Haley J. Comparison of hospitalizations, emergency room visits, fractures, and falls among parkinson disease patients who initiated therapy with selegiline or rasagiline: a retrospective study. Value in Health. 2013;16:A105.

[17] Delea TE, Thomas SK, Hagiwara M. The association between adherence to levodopacarbidopaentacapone therapy and healthcare utilization and costs among patients with parkinsons disease: A retrospective claims-based analysis. CNS Drugs. 2011;25:53-66.

[18] Wei YJ, Palumbo FB, Simoni-Wastila L, Shulman LM, Stuart B, Beardsley R, et al. Antiparkinson drug adherence and its association with health care utilization and economic outcomes in a Medicare Part D population. Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research. 2014;17:196-204.

[19] Kulkarni AS, Balkrishnan R, Anderson RT, Edin HM, Kirsch J, Stacy MA. Medication adherence and associated outcomes in medicare health maintenance organization-enrolled older adults with Parkinson's disease. Movement Disorders. 2008;23:359-65.

[20] Davis KL, Edin HM, Allen JK. Prevalence and cost of medication nonadherence in Parkinson's disease: evidence from administrative claims data. Mov Disord. 2010;25:474-80.

[21] PDMED Collaborative Group. Long-term effectiveness of dopamine agonists and monoamine oxidase B inhibitors compared with levodopa as initial treatment for Parkinson's disease (PD MED): a large, open-label, pragmatic randomised trial. The Lancet. 2014;384:1196-205.

[22] Grosset D, Antonini A, Canesi M, Pezzoli G, Lees A, Shaw K, et al. Adherence to antiparkinson medication in a multicenter European study. Mov Disord. 2009;24:826-32.

[23] Caslake R, Macleod A, Ives N, Stowe R, Counsell C. Monoamine oxidase B inhibitors versus other dopaminergic agents in early Parkinson's disease (Review). Cochrane Database Syst Rev 2009 CD006661. DOI: 10.1002/14651858.CD006661.pub2.

[24] Tomlinson C, Patel S, Meek C, Herd C, Clarke C, Stowe R, et al. Physiotherapy versus placebo or no intervention in PArkinson's disease (Review). Cochrane Database Syst Rev. 2013;CD002817. doi: 10.1002/14651858.CD002817.pub4.

[25] Iwamoto J, Sato Y, Takeda T, Matsumoto H. Strategy for prevention of hip fractures in patients with Parkinson’s disease. World Journal of Orthopedics. 2012;3:137-41.

[26] Tarantino U, Ortolani S, Degli Esposti L, Veronesi C, Buda S, Brandi M. Analysis of the costs and consequences of adherence to therapy in hip fracture patients. Results of a longitudinal analysis of administrative databases. Clin Cases Miner Bone Metab. 2011;8:57-62.

[27] Jarman B, Hurwitz B, Cook A, Bajekal M, Lee A. Effects of community based nurses specialising in Parkinson's disease on health outcomes and costs randomised controlled trial. BMJ. 2002;324:1072-5.

[28] Thomas R, Huntley A, Mann M, Huws D, Paranjothy S, Elwyn G, et al. Specialist clinics for reducing emergency admissions in patients with heart failure: a systematic review and meta-analysis of randomised controlled trials. Heart. 2013;99:233-9.

[29] Viswanathan M, Kahwati LC, Golin CE, Blalock SJ, Coker-Schwimmer E, Posey R, et al. Medication Therapy Management Interventions in Outpatient Settings: A Systematic Review and Meta-analysis. JAMA internal medicine. 2014;175:76-87.

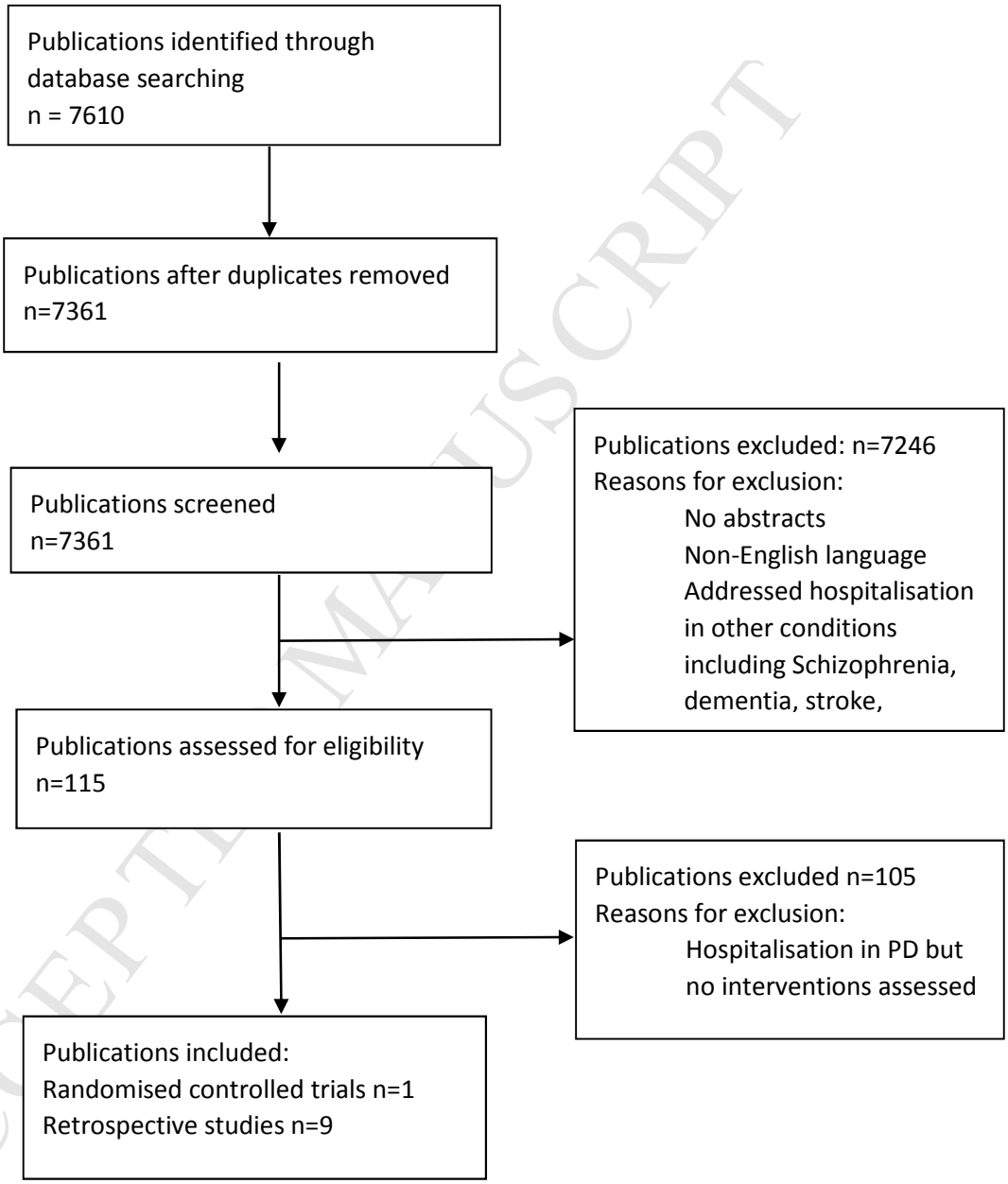
[30] Gibson P, Powell H, Wilson A, Abramson M, Haywood P, Bauman A, et al. Self-management education and regular practitioner review for adults with asthma (Review). Cochrane Database Syst Rev 2003. 2003;1:CD001117.

Table 1: Proposed interventions for reducing Parkinson's disease hospital admissions.

Proposed intervention Author, year	**Study type**	**Study Group**	**Study intervention**	**Outcome**	**Effect of proposed intervention on hospitalisation and emergency room visits**
Dysphagia management					
Robbins *et al* 2008[20]	Randomised Controlled Trial	515 (PD and dementia patients)	Chin down posture versus honey/nectar thick fluid	Pneumonia incidence, **Hospitalisation measured as an adverse event**	No difference in serious adverse events (including hospitalisation) between the two intervention grroups
Frequent Neurologist involvement					
Willis *et al 2012[11]*	Retrospective cohort	24929 PD patients	Neurologist versus no neurologist care	**PD-related and general medical related hospitalisation**	Neurologist care associated with ↓ hospitalisation for traumatic injury (HR 0.56, 95% CI 0.40-0.78), psychosis (HR 0.71, 95% CI 0.59-0.86) and urinary tract infection (HR 0.74 95% CI 0.63-0.87).
Ney *et al 2013[12]*	Survey	3883 Parkinsonism, multiple sclerosis, epilepsy, dementia.	Neurologist ambulatory care	Utilization and cost of non-ambulatory care : **inpatient, emergency**, and home care	↓ in condition related emergency, inpatient, and homecare care events (OR 0.64, P=0.001) and costs (53% ,p<0.001)
Open acess clinic					
Klein *et al* 2009[13]	Retrospective	143 PD patients	Open access clinie	**Mean number of hospitalisations per year, mean length of stay**	50% ↓ in average number of PD admissions over 2 years : 36 to 18
PD medication choice					
Grubb *et al 2012[14]*	Retrospective	7230 PD patients	Rasagiline versus dopamine agonists	**Number of hospitalisation, duration of stay and costs**	Fewer hospital admissions (OR 0.76, 95% CI 0.66-0.86), shorter length of stay and lower costs in rasagiline group
Grubb *et al 2013[15]*	Retrospective	3864 PD patients	Rasagiline versus Selegiline	**Hospitalisation, emeregency room visits and falls**	Lower emergency room visits (odds ratio: 0.79; 95% CI, 0.68 to 0.92), lower all hospital admissions (odds ratio: 0.82; 95% CI, 0.68 to 0.99), and lower number of falls in rasagiline group

PD Mediation Adherence					
Delea *et al 2011[16]*	Retrospective	1215 PD patients	Adherence to levodopa/carbidopa/ entacopone	**All cause and PD- related hospitalisations, length of stay, emergency room** and physicians visits, prescriptions and healthcare costs	Satisfactory adherence versus non adherent: mean number PD related admissions (0.15 vs 0.12 ,p<0.001), emergency visits (0.04vs 0.08, p=0.010), all cause hospitalisation (0.30 vs 0.53, p<0.001)
Kulkarni *et al 2008[18]*	Retrospective Longitudinal cohort	104 PD patients	PD medication adherence	Medication adherence, **PD related hospitalisations and emergency room visits.**	Suboptimal adherence associated with worsening motor symptoms: Odds for adherers (MPR>0.8) experiencing symptom worsening compared to non-adherers was 67% less (odd ratio 0.33 95% CI 0.13-0.85)
Wei *et al 2014[17]*	Retrospective Crossectional study	7583 PD patients	PD medication adherence	**Hospital visits, emergency room visits** , skilled nursing facility, home health agency, physcians visit and health costs	Prevalence and relative risk (low versus high adherers): hospitalisation 57% vs 47% and 1 versus 0.86 (95% CI 0.81-0.90), Emergency room visits 68% vs 59% and 1 versus 0.91(95% CI 0.86-0.96)
Davis *et al 2010[19]*	Retrospective	3119 PD patients	PD medication adherence	Medication adherence, health care utilisation (**including hospital admissions and emergency room visits**), and costs	Mean hospitalisation per annum, non-compliant versus compliant: 2.3 versus 1.8; p<0.005. Mean number of emergency departments visits were not significantly different 1.9 versus 1.8

Figure 1 : Flow diagram showing publications identified through database searching and reasons for inclusion and exclusion from the review



Highlights

- Hospitalisation in Parkinson's disease (PD) is a significant cost driver.
- We reviewed the literature for interventions aimed at reducing hospitalisation in PD
- There is a lack of robust evidence for interventions to reduce PD hospitalisation
- Open access PD clinics, regular neurologist care and PD symptoms control may mitigate non-elective PD admissions.