Title: Factors associated with Hospitalisation among people with Parkinson's disease – A Systematic Review and Meta-analysis.

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Keywords: Parkinson's disease; Hospitalisation; Factors; Prevalence; Admissions

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Abstract:

Introduction: Parkinson's disease (PD) is associated with an increased risk of admission to hospital, however data on the main reasons for admission is lacking. Our objective was to determine the pooled prevalence of the most common factors leading to admissions among people with Parkinson's disease.

Methodology: A systematic literature search was conducted in 11 electronic databases. We included all studies providing reasons for admissions among PD patients without restrictions to diagnostic criteria of PD, language or year of study. In the included studies, methodological quality, publication bias and heterogeneity were assessed. Meta-analysis was performed using random-effects models to calculate the pooled estimates of the identified top factors that lead to admission among people with PD.

Results: A total of 7283 studies were identified of which nine studies including 7162 people with PD were included in this review. There was a high degree of heterogeneity between studies regarding reasons for hospitalization. The pooled prevalence of the topmost reasons for hospitalisation among people with PD was 22%(95%CI 16.0%-30.0%) for infections (mainly urinary tract infections and pneumonia); 19%(95%CI 13.0%-27.0%) for worsening motor manifestations of PD; 18%(95%CI 14.0%-21.0%) for falls/fractures; 13%(95%CI 9.0%-18%) for cardiovascular co-morbidities; 8%(95%CI 4.0%-13.0%) for neuropsychiatric and 7%(95%CI 4.0%-11.0%) gastrointestinal complications.

Conclusion: The main reasons for hospitalisation among people with PD are infections, worsening motor features, falls/fractures, cardiovascular co-morbidities, neuropsychiatric and gastrointestinal complications. Further research is needed in targeting and implementing preventative strategies.

Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disease with prevalence ranging from 31-328 per 100,000 people worldwide [1]. These figures are expected to rise as life expectancy is increasing. The number of people with PD has been predicted to double by the year 2030 and so is the burden of the disease [2, 3].

Parkinson's disease is characterised by motor features (such as tremor, rigidity, postural instability and bradykinesia) and non-motor features such as pain, sleep disorders, autonomic dysfunction, mood disturbances and cognitive impairment.[4] As the disease progresses, these symptoms worsen resulting in increasing disability and deterioration in the patient's health status, leading to rising rates of hospital admissions. These in turn are associated with worse outcomes and increased societal costs [5-10]. The rate of hospitalisation among people with PD has been reported to be 1.44 times higher than that of age and sex-matched controls [11]. Pressley et al, in their study reported that people with PD were 1.5 times more likely to be hospitalised than individuals without PD [12].

An earlier review [13] considered the factors that may be important, but to our knowledge there has been no rigorous systematic review that synthesized data on pooled prevalence of identified reasons for admission. Identification of the factors associated with admissions in patients with PD could therefore help assess where

hospital admissions may be prevented. This could lead to a decrease in the mortality and morbidity associated with PD and reduce financial burden on the patients and healthcare system [14]. We therefore conducted a systematic review and meta-analysis regarding hospitalisation among people with PD to synthesize pooled estimates of prevalence of the common causes of admissions among these patients.

Methods

Source of data and search strategy

This study followed a pre-specified protocol throughout, utilizing the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines for the search, extraction, synthesis of results and reporting [15]. The protocol was registered on PROSPERO. One reviewer (OO) conducted searches of eleven electronic databases- MEDLINE (OVID), EMBASE, Web of science, Science Citation Index Expanded (SCIE), Cochrane Database of Systematic Reviews (CDRS), Cochrane Central Register of Controlled Trials (CCRCT), PsycINFO, Health Technology Assessment (HTA) database, NHS Health Economic Evaluation Database (HEED), Database of Abstracts of Reviews of Effects (DARE), Cumulative Index to Nursing and Allied Health Literature (CINAHL) initially in April 2018, updated October 2019. In order to maximize the sensitivity of the search, Medline Medical Subject Headings (MESH) and keyword terms were used where appropriate. There were no restrictions to language, diagnostic criteria of PD or year of publication.

The Parkinson's related search terms were "Parkinson" OR Parkinsonian disorder (MESH) AND the following admission-related terms: hospitalization (MESH) OR "hospitalisation" OR "Inpatient care" OR "admission(s)", Inpatients (MESH) OR

"patient admission" OR "patient readmission". (supplementary material: appendix 1)

This search was first run on Medline and then all other databases. Forwards and backwards citation tracking of key articles to identify other relevant studies was conducted.

Inclusion and Exclusion criteria

Original prospective or retrospective studies with any design were considered potentially eligible if the participants had PD and if the studies provided data on any form of hospitalization and reported reasons for admission among people with PD. Articles were excluded if they did not report reasons for admission or did not report the number admitted for each reason. Expert opinions, letter to the editor, casereports, editorials, and reviews were also excluded.

When data were collected from people with PD attending a hospital, the PD population was termed hospital-based. Studies which were community-based prevalence studies or involved national databases were designated as population-based [16, 17].

Studies were considered retrospective if data were collected by tracing and reviewing patients' files [18, 19] or codes were used to get PD patients information from electronic databases [20]. Prospective studies had to have used a pre-designed proforma used to collect data on admission [14, 16]

Study Selection

One investigator (OO) initially screened study title and abstracts for potentially eligible studies using the inclusion and exclusion criteria. The full texts of the selected articles were independently read as a whole and screened for eligibility by

two reviewers (OO, GK). Discrepancies were resolved through discussion with the whole team (OO, GK, KW and AS). Full text articles related to relevant conference abstracts retrieved were sought by additional database searching.

Data extraction

A standardized data extraction form was used to capture data of interest. These included: socio-demographic characteristics of the study participants; information on first author; cohort/study name; year of publication; country; study design; study population; proportion of males and females; mean age of subjects/controls; total number of admissions/hospitalisation; mean length of hospital stay; reasons/factors examined for admission; number of people with PD admitted for the different reasons; type of statistical analysis done; any interventions/preventive strategies delivered within each study and the outcome of hospitalisation where reported.

Methodological quality

The Newcastle-Ottawa scale [21] for case-control and cohort studies was used to assess the quality of the studies investigating factors associated with hospitalisation among people with PD. This was used to assess whether studies showed clarity on: the selection of population of interest, quantitative methodology, accuracy of recruitment process, data collection method and assessment of outcome. A total potential score of 0 to 9 was awarded, with a score of 0 to 3, 4-6 and 7 to 9 representing low, medium, and high-quality studies respectively. Studies were not excluded on the basis of quality, given the paucity of available data. (supplementary material: table 1)

Statistical analysis

In order to calculate the pooled prevalence of the common factors for admission through a meta-analysis, the exact number of people with PD in an entire cohort and the number admitted for each factor were extracted from each included study and used for the analysis.

In order to identify possible bias within the categories of studies that reported top factors for admission among people with PD, we assessed publication bias using the Egger's test. The degree of heterogeneity was assessed, using the *P* statistic. A value of 50% and more was considered significant [22].

The pooled prevalence of each of the common factors for admission among people with PD was calculated using a random-effects model since there was significant degree of heterogeneity between included studies. All statistical analyses were conducted using STATA 15.0 (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC).

Results

Selection processes

As shown in Figure 1, the electronic search of eleven databases identified 7283 studies. After removing 2436 duplicates, 4847 records identified by systematic search were screened. The full text articles of 65 studies were then assessed for eligibility, and of these 56 articles were excluded with reasons. Twenty-three [11, 16, 17, 20, 23-41] of the 56 excluded articles reported reasons for admission among people with PD but did not report exact number of people admitted for the reasons they reported so were excluded. (supplementary material: table 2) Finally, data were

captured from a total of nine articles: [14, 18, 19, 42-47]. The quality assessment showed that six [14, 18, 42, 44-46] of the studies were of moderate quality, while the remaining three [19, 43, 47] were high quality. (supplementary material: table 1)

General characteristics of selected studies

Of the nine articles included in this review, seven originally set out to investigate hospital admissions as well as reasons for admissions among people with PD while the others did not set out to investigate hospital admissions but included PD admissions as a sub-analysis. Six [18, 19, 42, 43, 45, 47] of the studies included were retrospective while three [14, 44,46] were prospective studies. There were three studies from Europe [43, 44, 46], two from the Middle East [19, 45] and one each from Australia [42], India [14] and Asia [18] and the United States of America [47]. One [42] of the articles included was a population-based study while the other eight [14,18, 19, 43-47] were hospital-based studies with most settings being emergency, general medicine and neurology departments (Table 1).

Reasons for Admission

Factors associated with hospitalisation among people with PD were classified variably by the authors as directly related to PD (PD-related) or indirectly related to PD (non PD-related) [14, 18, 19, 42, 44, 46, 47]. Others made no distinction [43, 45]. Factors directly related to PD according to the authors were mainly motor features ranging from uncontrolled motor features, prolonged "off" and frequent freezing, "On" and "Offs", dyskinesias and fluctuations. Factors which were not directly related to PD (non-PD related) included infections (urinary tract infection and pneumonia); cardiovascular comorbidities such as congestive cardiac failure, arrhythmias,

angina, ischaemic heart disease/acute coronary syndrome; cerebrovascular accident, transient ischaemic attack; syncope, postural hypotension; falls/fractures; encephalopathy, delirium electrolyte imbalance; rehabilitation; neoplasms; gastrointestinal issues: constipation, dysphagia, nausea and vomiting; neuropsychiatric problems: hallucinations and depression. (supplementary material: table 3).

The main reasons for hospital admissions among people with PD reported by all nine studies included were 1) infections (urinary tract infection and pneumonia);

2) gastrointestinal disorders; 3) falls/fractures; 4) PD related motor symptoms; 5) neuropsychiatric problems and 6) CVS comorbidities).

Prevalence of the common factors for admission in PD

All nine [14, 18, 19, 42-47] included studies reported the exact number of people with PD in their cohort and the number admitted for each factor (falls/fractures, infections, worsening symptoms of PD, cardiovascular comorbidities, gastrointestinal and neuropsychiatric symptoms) associated with admission among people with PD. Data from these nine studies were used to calculate the pooled prevalence of the common factors for admission in people with PD, through a meta-analysis. (Table 2)

The overall I² values for the nine studies based on each reported factor was high suggesting significant heterogeneity between studies. Studies which reported neuropsychiatric problems, worsening motor symptoms, infection and gastrointestinal problems had the highest I² values of 95.45%, 94.61%, 93.11%, 93.07% respectively. In addition, studies which reported cardiovascular comorbidities had I² value of 86.70% while those which reported falls/fractures had I² values of 78.63%. (Table 3)

The pooled prevalence of infections among eight studies was 22.0% (95% CI 16.0%-30.0%); that of worsening motor symptoms of PD among seven studies was 19.0%(95% CI 13.0%-27.0%); fall/fractures among seven studies was 18.0%(95% CI 14.0%-21.0%); cardiovascular co-morbidities among six studies was 13.0% (95% CI 9.0%-18.0%); neuropsychiatric symptoms among seven studies was 8.0% (95% CI 4.0%-13.0%) and that of gastrointestinal problems among eight studies was 7.0% (95% CI 4.0%-11.0%). (Table 4) (supplementary material: appendix 2)

Publication bias

According to the Egger's test there was no evidence of publication bias in all the study outcomes (all p>0.05) except worsening motor features of PD (p=0.013). This could be accounted for by the heterogeneity of the study population. (Table 4) (supplementary material: appendix 2)

Discussion

This systematic review and meta-analysis summarises the reported factors associated with admissions in people with PD and suggests that the main causes of hospitalisation among people with PD are infections, particularly urinary tract infection (UTI) and pneumonia, worsening motor features, falls/fractures, cardiovascular comorbidities, gastrointestinal complications (constipation, dysphagia, nausea and vomiting) and neuropsychiatric problems which included hallucinations, psychosis and depression. Although there is no meta-analysis or prevalence data to compare with, our findings are in line with a recent systematic review which reported falls, acute decompensation of PD symptoms, cardiovascular comorbidities and

infections as accounting for more than 50% of admissions among people with PD. However, the exact prevalence of these causes was not defined [13]. Infections, mainly UTI and pneumonia were the topmost reason for admission among people with PD. This supports data provided by a number of other studies which identified infectious diseases including aspiration pneumonia, UTI and others as common reasons for emergency admissions [14, 31, 45, 48]. In contrast, falls/fractures are the most reported in other studies. The explanation for this discrepancy may be that infections are underestimated in some studies by reporting UTI under urinary disorders and not as an infection. Conversely, people with PD may have falls resulting from a deterioration due to UTI which could be coded as falls [18, 18, 26]. In terms of underlying reasons, bladder emptying problems due to autonomic dysfunction in PD can lead to UTI among people with PD. In addition, bowel problems causing constipation and faecal impaction can lead to retention and subsequent urinary tract infection [49]. Pneumonia, which is reported to be one of the most common causes of death among people with end stage PD [50, 51], can be the consequence of swallowing difficulties, poor cough and poor respiratory effort as the disease progresses leading to recurrent aspiration and then pneumonia [52, 53]. It is therefore important to recognise these predisposing factors early and institute treatment in order to avoid hospitalisation.

Worsening motor manifestations of PD was the second main reason for hospitalisation among people with PD. These ranged from uncontrolled motor features, prolonged "off" and frequent freezing, "On" and "Offs", dyskinesias, fluctuations and medication side effects, all which result in increased morbidity in people with PD. This is in line with a systematic review which reported acute deterioration of motor symptoms as the second most common cause of

admission. Again, careful out-patient based titration of medications may pre-empt a deterioration of motor complications leading to admission.

Falls and fractures were the third most common reason for admission among people with PD. Falls with or without fractures have also previously been reported as a major reason for admission among people with PD and as a main cause of morbidity, reduced quality of life and increase in mortality [53, 54]. Postural instability, gait abnormalities and postural hypotension may underlie the occurrence of falls in PD, and they may occur as a consequence of UTI or motor deterioration in people with PD [54]. Therefore, evaluation and intervention by community or hospital-based physiotherapists trained in PD may lead to a reduction in falls among people with PD [53, 55, 56].

Cardiovascular co-morbidities (such heart failure and acute coronary syndrome/myocardial infarction) were the fourth common reason for hospital admission. Whilst cardiovascular risk has been reported to be increased in PD[12], they are also common in the general population in this age group [11]. Only two of the included studies had a control group, to allow for comparison of excess risk in people with PD[42, 43]. Cardiovascular diseases were reported to be less represented among people with PD in these cohorts compared to age and sex matched control [42, 43].

Neuropsychiatric manifestations were the fifth reason for admissions among people with PD. Neuropsychiatric features are common non-motor manifestations of PD and can be considered as part of the PD spectrum [42]. These include hallucinations and delusions which may be medication-induced. Therefore, careful use of medications that can precipitate such neuropsychiatric complications such as those with anticholinergic properties should be advised [11, 19, 43, 46].

Gastrointestinal problems which were mainly constipation, dysphagia, nausea and vomiting are the last category of reasons for hospital admissions among people with PD. When compared with a control group weighted for age and gender distribution, people with PD were more than twice more likely to require an admission for management of gastrointestinal problems [42]. People with PD require careful monitoring in order to recognise and promptly treat these complications. Treatment of constipation, changes to dietary consistency and swallowing assessment may help prevent these complications [13]. Gastrointestinal disturbances, falls/trauma, delirium, infections, genitourinary and electrolyte disturbances were reported as indirect reasons for admission which become more troublesome as PD progresses [14]. In addition, as life expectancy of people with PD increases, the rate of complications due to advancing disease as well as the hospital admissions also increase [14]. It is therefore imperative to develop pathways for early recognition of the identified reasons for admission in PD and for easy access to appropriate care either in the community or hospital in order to reduce unwarranted hospitalisation. The focus of future research should be to determine the clinical and cost effectiveness of preventive strategies addressing these key reasons in order to reduce hospital admissions among people with PD.

Strengths and Limitations

The main strength of this review is the robust and reproducible methodology. This involved using multiple databases with extensive search terms, the use of two reviewers to conduct the screening and assessment of inclusion and exclusion criteria and adherence to PRISMA guidelines. In addition, this was the first study to quantitatively pool the prevalence of the common factors associated with admissions in PD using meta-analysis methods.

The main limitation of this study's results is the limited number of high quality studies found. Many of the studies did not report the exact number of people with PD and reasons for admission and so were not included in the meta-analysis. In addition, we have relied on the authors reported categorisation of reasons for admission, and there may be inaccuracies in this.

Conclusion

This is the first meta-analysis on the prevalence of common factors that lead to hospitalisation among people with PD. We provide prevalence estimates for the main reasons for hospital admissions, to facilitate subsequent research on these factors to prevent admission among people with PD. Infections, worsening motor features, falls/fractures, cardiovascular co-morbidities, neuropsychiatric and gastrointestinal problems were the most common reasons for admission.

Understanding and implementing preventive strategies for these key contributors of hospital admission has the potential to reduce hospital admission and thereby improve the quality of life of people with PD and reduce burden on healthcare system.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or non-for-profit sectors

Author contributions

OO and AS developed the concept for the study. OO carried out search, quality assessment and initial data interpretation. GK was second reviewer. OO and GK carried out statistical analysis. OO prepared the manuscript draft, with input and revisions from AS, KW and LM. All authors approved the final version.

Acknowledgements

We would like to acknowledge Jennifer Ford of the UCL, Royal Free Hospital Medical Library for her bibliographic assistance.

References

- 1. C. Tanner, Early Intervention in Parkinson's Disease: Epidemiologic Considerations, Ann Epidemiol. 6 (1996) 438-441.
- 2. E. Dorsey, R. Constantinescu, J. Thompson, K. Biglan, R. Holloway, K. Kieburtz, F. Marshall, B. Ravina, G. Schifitto, A. Siderowf, C. Tanner, Projected number of people with PD, Parkinson disease in the most populous nations, 2005 through 2030, Neurology. 68 (2007) 384-386.
- 3. S.M. Khandhar, W.J. Marks, Epidemiology of Parkinson's disease, Dis Mon. 53(4) (2007) 200-205.
- 4. L.V. Kalia, A.E. Lang, Parkinson's disease, The Lancet, 386(9996) (2015) 896-912.
- 5. M. Guttman, P. Slaughter, M. Theriault, D. DeBoer, C. Naylor, Burden of Parkinsonism: A Population-Based Study, Movement Disorders. 18(3) (2003) 313-336.
- 6. R. Scheife, G. Schumock, A. Burstein, M. Gottwald, M. Luer, Impact of Parkinson's disease and its pharmacologic treatment on quality of life and economic outcomes, Am J Health-Syst Pharm, 57 (2000) 953-962.
- 7. R. Dodel, M. Singer, R. Kohne-Volland, T. Szucs, B. Rathay, E. Scholz, W. Oertel, The Economic Impact of Parkinson, Pharmacoeconomics. 14(3) (1998) 299-312.
- 8. L. Rubenstein, E. Chrischilles, M. Voelker, The Impact of Parkinson's Disease on Health Status, Health Expenditures, and Productivity Estimates from the National Medical Expenditure Survey, Pharmacoeconomics.12(4) (1997) 1170-7690.
- 9. K. Whetten-Goldstein, F. Sloan, E. Kulas, T. Cutson, M. Schenkman, The Burden of Parkinson's disease on society, family, and individual. Journal of the American Geriatrics Societ. 45(7) (1997) 844-849.
- 10. E. Singer, Social costs of Parkinson's disease, J Chronic Dis. 26 (1973) 243-254.
- 11. M. Guttman, P.M. Slaughter, M.E. Theriault, D.P. DeBoer, C.D. Naylor, Parkinsonism in Ontario: comorbidity associated with hospitalization in a large cohort, Movement Disorders. 19(1) (2004) 49-53.
- 12. J.C. Pressley, E.D. Louis, M.-X. Tang, L. Cote, P.D. Cohen, S. Glied, R. Mayeux, The impact of comorbid disease and injuries on resource use and expenditures in parkinsonism, Neurology. 60 (2003) 87-93.
- 13. L. Koay, J. Rose, A.H. Abdelhafiz, Factors that lead to hospitalisation in patients with Parkinson disease. A systematic review, International Journal of Clinical Practice. 72 2018) 5.
- 14. B.S. Paul, G. Paul, G. Singh, S. Kaushal, U. Verma, Pattern of hospital admission and outcome in Parkinson's disease: A study from Punjab, India. Neurology Asia. 22(1) (2017) 33-39.
- 15. D. Moher, A. Liberati, J. Tetzlaff, D.G. Altman, P. Group, Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 6(7) (2009) e1000097.
- 16. C. Vossius, O. Nilsen, J. Larsen, Parkinson's disease and hospital admissions: Frequencies, diagnoses and costs, Acta Neurologica Scandinavica. 121(1) (2010) 38-43.

- 17. B. Kelly, C. Blake, O. Lennon, Acute Hospital Admissions of Individuals with a Known Parkinson's Disease Diagnosis in Ireland 2009-2012: A Short Report. Journal of Parkinsons Disease Print. 6(4) (2016) 709-716.
- 18. L.C. Tan, A.K. Tan, H.T. Tjia, The profile of hospitalised patients with Parkinson's disease, Annals of the Academy of Medicine Singapore. 27(6) (1998) 808-12.
- 19. C. Klein, T. Prokhorov, A. Miniovitz, E. Dobronevsky, J.M. Rabey, Admission of Parkinsonian patients to a neurological ward in a community hospital. Journal of Neural Transmission. 116(11) (2009) 1509-12.
- 20. U. Lertxundi, A. Isla, M.A. Solinis, S.D. Echaburu, R. Hernandez, J. Peral-Aguirregoitia, J. Medrano, J.C. Garcia-Monco, Medication errors in Parkinson's disease inpatients in the Basque Country. Parkinsonism & Related Disorders, 36 (2017) 57-62.
- 21. G. Wells, B. Shea, D. O'connell, J. Peterson, V. Welch, M. Losos, P. Tugwell, The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses, Ottawa Hospital Research Institute, 2014. 2015, oxford. ASp.
- 22. J. Higgins, S. Thompson, J. Deek, D. Altman, Measuring inconsistency in meta-analyses, BMJ, 327(7414) (2003) 557-560.
- 23. H. Woodford, R. Walker, Emergency hospital admissions in idiopathic Parkinson's disease. Movement Disorders, 2005. 20(9): p. 1104-1108.
- 24. L. Shahgholi, S. De Jesus, S.S. Wu, Q.L. Pei, A. Hassan, M.J. Armstrong, D. Martinez-Ramirez, P. Schmidt, M.S. Okun, Hospitalization and rehospitalization in Parkinson disease patients: Data from the National Parkinson Foundation Centers of Excellence, Plos One. 12(7) (2017) 10.
- 25. M. Harris, M. Fry, The utilisation of one district hospital emergency department by people with Parkinson's disease, Australasian Emergency Nursing Journal. 20(1) (2017) 1-5.
- 26. J.A Temlett, P.D. Thompson, Reasons for admission to hospital for Parkinson's disease. Internal Medicine Journal. 36(8) (2006) 524-526.
- 27. A. Merola, R.P. Sawyer, C.A. Artusi, R. Suri, Z. Berndt, J.R. Lopez-Castellanos, J. Vaughan, J.A. Vizcarra, A. Romagnolo, A.J. Espay, J.R. Lopez-Castellanos, Orthostatic hypotension in Parkinson disease: Impact on health care utilization. Parkinsonism & Related Disorders. 47 (2018) 45-49.
- A. Mahajan, P. Balakrishnan, A. Patel, I. Konstantinidis, D. Nistal, N. Annapureddy, P. Poojary, G.N. Nadkarni, C. Sidiropoulos, Epidemiology of inpatient stay in Parkinson's disease in the United States: Insights from the Nationwide Inpatient Sample, Journal of Clinical Neuroscience. 31 (2016) 162-5.
- 29. R. Gil-Prieto, R. Pascual-Garcia, J. San-Roman-Montero, P. Martinez-Martin, J. Castrodeza-Sanz, A. Gil-de-Miguel, Measuring the Burden of Hospitalization in Patients with Parkinson's Disease in Spain, PLoS ONE [Electronic Resource]. 11(3) (2016) e0151563.
- 30. D. Martinez-Ramirez, L. Almeida, J.C. Giugni, B. Ahmed, M. Higuchi, C.S. Little, J.P. Chapman, C. Mignacca, A.W. Shukla, C.W. Hess, K.W. Hegland, M.S. Okun, Rate of aspiration pneumonia in hospitalized Parkinson's disease patients: a cross-sectional study. Bmc Neurology. 15 (2015) 6.
- 31. V. Low, Y. Ben-Shlomo, E. Coward, S. Fletcher, R. Walker, C.E. Clarke, 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. 21(5) (2015) 449-54.
- 32. E.D. Louis, C. Henchcliffe, B.T. Bateman, C. Schumacher, Young-onset Parkinson's disease: hospital utilization and medical comorbidity in a nationwide survey, Neuroepidemiology. 29(1-2) (2007) 39-43.
- 33. O.H.H. Gerlach, M.P.G. Broen, P.H.M.F. van Domburg, A.J. Vermeij, W.E.J. Weber, Deterioration of Parkinson's disease during hospitalization: Survey of 684 patients. BMC Neurology. (2012) 13.
- 34. A.W. Willis, M. Schootman, R. Tran, N. Kung, B.A. Evanoff, J.S. Perlmutter, B.A. Racette, A.W. Willis, M. Schootman, R. Tran, N. Kung, B.A. Evanoff, J.S. Perlmutter, B.A. Racette, Neurologist-associated reduction in PD-related hospitalizations and health care expenditures, Neurology. 79(17) (2012) 1774-1780.
- 35. K.L. Chou, J. Zamudio, P. Schmidt, C.C. Price, S.A. Parashos, B.R. Bloem, K.E. Lyons, C.W. Christine, R. Pahwa, I. Bodis-Wollner, W.H. Oertel, O. Suchowersky, M.J. Aminoff, I.A. Malaty, J.H. Friedman, M.S. Okun, K.L. Chou, J. Zamudio, P. Schmidt, and C.C. Price, Hospitalization in Parkinson disease: a survey of National Parkinson Foundation Centers. Parkinsonism & Related Disorders. 17(6) (2011) 440-445.
- 36. M.Cosentino, E. Martignoni, D. Michielotto, D. Calandrella, G. Riboldazzi, C. Pacchetti, G. Frigo, G. Nappi, S. Lecchini, Medical healthcare use in Parkinson's disease: survey in a cohort of ambulatory patients in Italy. BMC Health Services Research. 5(1) (2005) 26.
- 37. R.W. Walker, J. Palmer, J. Stancliffe, B.H. Wood, A. Hand, W.K. Gray, Experience of care home residents with Parkinson's disease: Reason for admission and service use, Geriatrics & gerontology international. 14(4) (2014) 947-53.
- 38. C.P. Derry, K.J. Shah, L. Caie, C.E. Counsell, Medication management in people with Parkinson's disease during surgical admissions, Postgraduate Medical Journal. 86(1016) (2010) 334-337.
- 39. J. Martins, A. Rua, N.V. Cha, Hospital Mortality in Parkinson's Disease: Retrospective Analysis in a Portuguese Tertiary Centre, Acta Medica Portuguesa. 29(5) (2016) 315-318.
- 40. S. Muzerengi, , C. Rick, I. Begaj, N. Ives, F. Evison, R.L. Woolley, C.E. Clarke, Coding accuracy for Parkinson's disease hospital admissions: implications for healthcare planning in the UK. Public Health. 146 (2017) 4-9.
- 41. P. Hobson, S. Roberts, G. Davies, The introduction of a Parkinson's disease email alert system to allow for early specialist team review of inpatients, BMC Health Services Research. 19(1) (2019) 271.
- 42. M. Lubomski., R.L. Rushworth, S. Tisch, Hospitalisation and comorbidities in Parkinson's disease: a large Australian retrospective study, Journal of Neurology, Neurosurgery & Psychiatry. 86(3) (2015) 324-30.
- 43. M. Braga, M. Pederzoli, A. Antonini, F. Beretta, V. Crespi, Reasons for hospitalization in Parkinson's disease: a case-control study. Parkinsonism & Related Disorders. 20(5) (2014) 488-492; discussion 488.
- 44. R. Skelly, L. Brown, A. Fakis, L. Kimber, C. Downes, F. Lindop, C. Johnson, C. Bartliff, N. Bajaj, Does a specialist unit improve outcomes for hospitalized patients with Parkinson's disease? Parkinsonism & Related Disorders. 20(11) (2014) 1242-1247.

- 45. O.Guneysel, O. Onultan, O. Onur, Parkinson's disease and the frequent reasons for emergency admission. Neuropsychiatric Disease & Treatment. 4(4) (2008) 711-714.
- 46. E. Martignoni, L. Godi, A. Citterio, R. Zangaglia, G. Riboldazzi, D. Calandrella, C. Pacchetti, G. Nappi, D. Porazzi, F. Reverberi, G. Chiodelli, G. Guarneri, M.B. Zappacosta, G. Mariani, R. Freschi, F. Sasanelli, G. Molini, F. Shieroni, M. Di Costanzo, G. Bargnani, E. Donati, G. Bono, and E. Magrotti, Comorbid disorders and hospitalisation in Parkinson's disease: A prospective study. Neurological Sciences. 25(2) (2004) 66-71.
- 47. I.I. Kessler, Epidemiologic studies of Parkinson's disease. II. A hospital-based survey, American Journal of Epidemiology, 1972. 95(4): p. 308-18.
- 48. S. Fujioka, J. Fukae, H. Ogura, T. Mishima, S. Yanamoto, M.A. Higuchi, G. Umemoto, Y. Tsuboi, Hospital-based study on emergency admission of patients with Parkinson's disease, eNeurologicalSci. 4 (2016) 19-21.
- 49. O. Oguh, A. Videnovic, Inpatient management of Parkinson's disease: current challenges and future directions, Neurohospitalist 2(1) (2012) 28-35.
- 50. M. Beyer, K. Herlofson, D. Arsland, J. Larsne, Causes of death in a community-based study of Parkinson's disease. Acta Neurologica Scandinavica. 103 (2001) 7-11.
- 51. S. Pennington, K. Snell, M. Lee, R. Walker, The cause of death in idiopathic Parkinson's disease, Parkinsonism Relat Disord. 16(7) (2010) 434-437.
- 52. N. Leopold, M. Kagel, Laryngeal deglutination movement in Parkinson's disease. Neurology. 48 (1997) 373-375.
- 53. A. Arasalingam, C.E. Clarke, Reasons for Parkinson's disease admissions in a large inner city hospital. Parkinsonism Relat Disord. 20(2) (2014) 237-8.
- 54. A. Schrag, Y. Ben-Shlomo, N. Quinn, How common are complications of Parkinson's disease? J Neurol. 249 (2002) 419-423.
- 55. M. Munneke, M.J. Nijkrake, S.H.J. Keus, G. Kwakkel, H.W. Berendse, R.A.C. Roos, G.F. Borm, E.M. Adang, S. Overeem, B.R. Bloem, Efficacy of community-based physiotherapy networks for patients with Parkinson's disease: a cluster-randomised trial. The Lancet Neurology. 9(1) (2010) 46-54.
- 56. C.L. Tomlinson, S. Patel, C. Meek, C.P. Herd, C.E. Clarke, R. Stowe, L. Shah, C. Sackley, K.H. Deane, K. Wheatley, N. Ives, Physiotherapy intervention in Parkinson's disease: systematic review and meta-analysis, BMJ. 345 (2012) e5004.



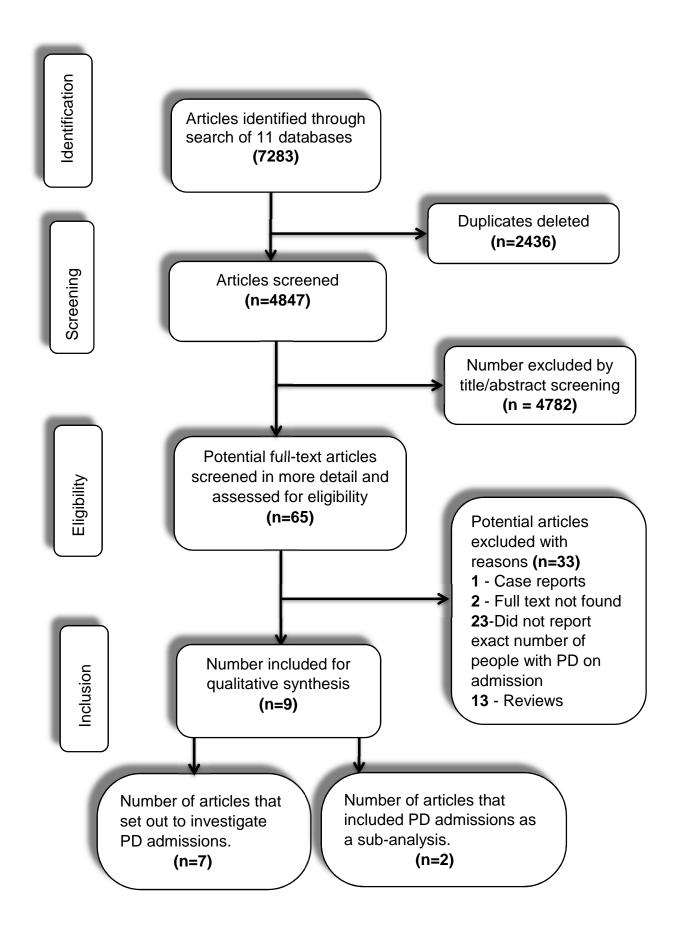


Table 1: General characteristics of included studies

Study	Year	Country	Study design	Aim of study	Cohort	Mean Age of PD cases	Female(%)	Main reasons for admission reported
Paul BS et al	2017	India	Prospective	Analyse causes for hospital admission	146	68.5	33.3%	Motor features & Levodopa related motor features, Infections, encephalopathy, fractures
Lubomski et al	2014	Australia	Retrospective	Examine patterns of acute care hospitalisation of PD cases	5637	75	37.2%	Falls/fractures, Cardiovascular problems, dementia.
Braga et al	2014	Italy	Retrospective	To detect co-morbid conditions in large population of PD cases.	295	76.7	Not reported	Neuropsychiatric disorders, cardiovascular problems, infections, medical problems, trauma- fracture.
Skelly et al	2014	United Kingdom (Derby)	Prospective	To confirm that care on a specialist inpatient PD Unit (SPDU) would improve outcomes of urgent medical care among PD cases.	44	81	26.5	PD symptoms, LRTI/pneumonia, UTI, postural hypotension.
Klein et al	2009	Israel	Retrospective	Review reasons for admission of PD cases to neurological department.	143	69.5	55	PD-motor and non- motor problems, falls, infections.

Table 1: General characteristics of included studies

Study	Year	Country	Study design	Aim of study	Cohort	Mean age of PD cases	Female(%)	Main reasons for admission reported
Guneysel et al	2008	Turkey	Retrospective	To determine reason for emergency admission	76	73.2	28	Infections(pneumonia, UTI), trauma(falls/fracture), Cardiovascular co- morbidities
Matignoni et al	2004	Italy	Prospective	To investigate acute comorbid events prompting hospitalisation	180	75.6	88	Drug monitoring, Trauma, Cardiovascular disorders, medical problems.
Tan et al	1998	Singapore	Retrospective	To provide profile of PD patients who required hospital admission	173	74.7	80	Uncontrolled PD symptoms, chest infections, urinary dysfunction, falls.
Kessler et al	1972	USA	Retrospective	Epidemiologic studies in PD.	468	Not reported	46	PD symptoms, cardiovascular, respiratory & digestive system problems.

Table 2: Data used for meta-analysis

	No of F with fal	•	No of with infection (UTI & pneum	· ·	with v	PD pts vorsening features	with cardio	PD pts vascular rbidities	No of with Gintestin	nal	with N psychi		Total no of PD cases in the study
_	No	%	No	%	No	%	No	%	No	%	No	%	No
Paul BS et al (2017)	13	8.9	25	17.1	47	32.2	18	12.3	3	2.1	4	2.7	146
Lubomski M et al (2014)	1116	19.8	1149	20.4	569	10.1	941	16.7	749	13.3	766	13.6	5637
Braga et al (2014)	47	15.9	59	20			29	9.8	16	5.4	18	6.1	295
Skelly et al (2014)			25	56.8	6	13.6							44
Klein et al (2009)	30	21	22	15.4	29	20.3			5	3.5	22	15.4	143
Guneysel et al (2008)	21	27.6	24	31.6			11	14.5	6	7.9			76
Matignoni et al (2004)	21	11.7	7	3.9	37	20.6	11	6.1	4	2.2	11	6.1	180
Tan et al (1998)	39	22.5	59	34.1	40	23.1	41	23.7	34	19.7	27	15.6	173
Kessler et al (1972)					91	19.4			45	9.6	10	2.1	468
Total no of articles with data on reason for admission	7		8		7		6		7		7		
1 ²	78.65%	, 0	93.119	%	94.61	%	86.7%	1	93.079	%	95.459	%	

Table 3: Reasons for hospital admissions in included studies

	Paul BS et al (2017)	Lubomski et al (2014)	Braga et al (2014)	Skelly et al (2014)	Klein et al (2009)	Guneysel et al (2008)	Matignoni et al (2004)	Tan et al (1998)	Kessler et al (1972)	l ² (%)
Neuropsychiatric problems (hallucinations, psychosis & depression)	√	√	√		√		√	√	✓	95.45%
Worsening motor features	√	√		✓	✓		✓	✓	√	94.61%
Infections (urinary tract infection & pneumonia)	✓	✓	✓	✓	\checkmark	√	✓	√		93.11%
Gastrointestinal complications (constipation, dysphagia, nausea and vomiting)		✓	✓		✓	√	✓	√	✓	93.07%
Cardiovascular co-morbidities (heart failure & acute coronary syndrome)	✓	✓	✓			✓	✓	✓		86.7%
Falls & fractures	√	√	√		√	√	√	√		78.65%

Table 4: Prevalence of the common factors for admission in PD

Topmost factors for admission	l ² (%)	Publication bias	Estimated Pooled prevalence (%)	Estimated Pooled prevalence (95% CI)	p-value	Studies
Infection (urinary tract infection & pneumonia)	93.11	0.597	22	16-30	<0.001	[14, 18, 19, 42-46]
Worsening motor features of PD	94.61	0.013	19	13-27	<0.001	[14, 18, 19, 42, 44, 46, 47]
Falls/fractures	78.63	0.473	18	14-21	<0.001	[14, 18, 19, 42, 43, 45, 46]
Cardiovascular co- morbidities (heart failure & acute coronary syndrome)	86.70	0.367	13	9-18	<0.001	[14, 18, 42, 43, 45, 46]
Neuropsychiatric complications Hallucinations, psychosis, & depression)	95.45	0.147	8	4-13	<0.001	[14, 18, 42, 43, 46, 47]
Gastrointestinal problems (constipation, dysphagia, nausea & vomiting)	93.07	0.058	7	4-11	<0.001	[14, 18, 42, 43, 45, 46]

Supplementary material: Appendix 1

Medline search

- 1. Parkinson*.mp. [mp= title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
- 2. exp Parkinsonian Disorders/
- 3. 1 or 2
- 4. hospitalization*.mp. [mp= title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
- 5. hospitalisation*.mp.
- 6. (inpatient* adj3 care).mp. [mp= title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
- 7. admission*.mp.
- 8. Inpatients/
- 9. (Patient* adj3 admission*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
- 10. (Patient* adj3 readmission*).mp.
- 11. exp Hospitalization/
- 12. 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
- 13. 3 and 12

Supplementary material, table 1 : Scoring of included studies (Newcastle-Ottawa scale scores)

Study	•	Case	Represen	Control	Control	Compara	Exposure	Same	Response	Total
ID		definition	tation	selection	definition	-bility	ascertain- ment	method of ascertainment	rate	score
1	Lubomski et al	b0	a1	b0	a1	a1b1	a1	b0	b0	5
2	Braga et al	a1	a1	b0	a1	a1b1	a1	a1	b0	7
3	Kessler et al	a1	a1	a1	a1	a0b0	a1	a1	a1	7
	Reference	Represen tation of exposed cohort	Selection of non- exposed cohort	Exposure Ascertain ment	Study outcome was not present at the start of study	Compara- bility	Outcome assessment	Was follow-up adequate to assess outcome	Adequacy of follow- up of cohorts	Total score
4	Paul BS et al	a1	c0	a1	a1	a0b0	a1	b0	a1	5
5	Skelly et al	a1	c0	a1	a1	a0b0	a1	b0	d0	4
6	Klein et al	a1	a1	a1	a1	a1b0	a1	a1	a1	8
7	Guneysel et al	a1	c0	a1	a1	a0b0	a1	b0	a1	5
8	Matignoni et al	a1	c0	a1	a1	a0b0	a1	b0	a1	5
9	Tan et al	a1	c0	a1	a1	a0b0	a1	b0	a1	5

Supplementary material, table 2: Reasons for exclusion of excluded studies

lementary material, table 2. Reasons for exclusion or excluded	Studies
Reasons for exclusion	
Lannon et al 1986. Comprehensive care of the patient with Parkinson's disease.	Review article
Trewin et al, 1997. Differences in drug prescribing patterns in elderly parkinsonian patients identified at hospital admission	Did not report reason for admission
Parashos SA et al, 2002. Medical services utilization and prognosis in Parkinson disease: a population-based study	Did not report reason for admission
Benbir G et al 2006. A hospital-based study: risk factors in development of motor complications in 555 Parkinson's patients on levodopa therapy	Reported risk factors
Doux, MM, 1993. Management of the hospitalized Parkinson patient	Full text not found
Escudero Torreila J, 1997. The medical care of patients with Parkinson's disease in a general hospital.	Full text not found
Magdalinou K et al, 2007. Prescribing medications in Parkinson's disease (PD) patients during acute admissions to a district general hospital.	Did not report reason for admission
Wood LD et al, 2010. Challenges of medication management in hospitalized patients with Parkinson's disease.	Commentary
Aminoff MJ et al, 2011. Management of the hospitalized patient with Parkinson's disease: current state of the field and need for guidelines	Review
Gerlach OH et al, 2011. Parkinson's disease and hospitalization: the need for guidelines.	Letter to the editor.
Jones SL et al, 2011. Parkinson's disease in the acute hospital.	Review
Donaldson S, 2010. Can we improve the inpatient care of those with Parkinson's disease?	Review
Stickley L 2009. Parkinson disease: current evidence for acute care management	Review
Eschie D, 2012. Patients with Parkinson's disease in hospital. [German].	Review
Hobson DE et al, 2012. Healthcare utilization in patients with Parkinson's disease: a population-based analysis.	Did not report reason for hospitalisation.
MacMahon MJ et al, 2012. Management of Parkinson's disease in the acute hospital environment.	Review
Oguh O et al, 2012. Inpatient management of Parkinson disease: current challenges and future directions.	Review
2013. Parkinson's inpatients criticise inflexible regimens in US study	News letter
Gombert C et al, 2013. Parkinson's disease and intensive care: Specific issues?. [French]	Review
	Reasons for exclusion Lannon et al 1986. Comprehensive care of the patient with Parkinson's disease. Trewin et al, 1997. Differences in drug prescribing patterns in elderly parkinsonian patients identified at hospital admission Parashos SA et al, 2002. Medical services utilization and prognosis in Parkinson disease: a population-based study Benbir G et al 2006. A hospital-based study: risk factors in development of motor complications in 555 Parkinson's patients on levodopa therapy Doux, MM, 1993. Management of the hospitalized Parkinson patient Escudero Torreila J, 1997. The medical care of patients with Parkinson's disease in a general hospital. Magdalinou K et al, 2007. Prescribing medications in Parkinson's disease (PD) patients during acute admissions to a district general hospital. Wood LD et al, 2010. Challenges of medication management in hospitalized patients with Parkinson's disease. Aminoff MJ et al, 2011. Management of the hospitalized patient with Parkinson's disease: current state of the field and need for guidelines Gerlach OH et al, 2011. Parkinson's disease and hospitalization: the need for guidelines. Jones SL et al, 2011. Parkinson's disease in the acute hospital. Donaldson S, 2010. Can we improve the inpatient care of those with Parkinson's disease? Stickley L 2009. Parkinson disease: current evidence for acute care management Eschie D, 2012. Patients with Parkinson's disease in hospital. [German]. Hobson DE et al, 2012. Healthcare utilization in patients with Parkinson's disease: a population-based analysis. MacMahon MJ et al, 2012. Management of Parkinson's disease in the acute hospital environment. Oguh O et al, 2012. Inpatient management of Parkinson disease: current challenges and future directions. 2013. Parkinson's inpatients criticise inflexible regimens in US study Gombert C et al, 2013. Parkinson's disease and intensive

20.	Arasalingam A et al, 2014. Reasons for Parkinson's disease	Letter to the
	admissions in a large inner city hospital.	editor
21.	Wijma-Vos L et al, 2014. Parkinson's short stay helps to	Dutch paper
	better set medication: Brief intervention is possible	(review)
	alternative before final admission. [Dutch]	
22.	Patel RS et al, 2017. Impact of Depression on	Did not report
	Hospitalization and Related Outcomes for Parkinson's	reason for
	Disease Patients: A Nationwide Inpatient Sample-Based	admission
	Retrospective Study.	
23.	Paul SS et al, 2017. Fall-related hospitalization in people	Reported only
	with Parkinson's disease.	falls
24.	Factor SA et al, 2000. Emergency department presentations	Case series
	of patients with Parkinson's disease.	
25.	Muzerengi S et al, 2016. Review of interventions to reduce	review
	hospitalisation in Parkinson's disease.	
26.	Queen V, 2017. Caring for patients with Parkinson's disease	review
	in general hospital settings	
27.	Clarke C et al, 2015. Emergency admissions, hospital stays	News
	and in-hospital mortality higher in patients with Parkinson's	
	disease.	
28.	2015. Parkinson's carries higher risk of dying after	News
	admission.	
29.	Straif-Bourgeois et al, 2015. Parkinson Disease	Did not report
	Hospitalizations and Mortality in Louisiana, 1999-2012.	reason for
		admission
30.	Chang Y et al, 2016. Risk factors for pneumonia among	Reported RFs
	patients with Parkinson's disease: A Taiwan nationwide	for
	population-based study.	development
		of pneumonia
31.	DiBartolo M et al, 2017. Enhancing Care for Hospitalized	Editorial
	Patients with Parkinson's Disease: Development of a Formal	
	Educational Program for Nursing Staff.	
32.	Koay, L. Factors that lead to hospitalisation in patients with	Review
	Parkinson disease-A systematic review.	
L	-	
33.	Munim F, 2017. Management of inpatients with Parkinson's	Algorithm
	disease in the acute setting.	

34.	M. Guttman, P.M. Slaughter, M.E. Theriault, D.P. DeBoer, C.D. Naylor, Parkinsonism in Ontario: comorbidity associated with hospitalization in a large cohort, Movement Disorders. 19(1) (2004) 49-53.	Did not report number admitted for what reason
35.	C. Vossius, O. Nilsen, J. Larsen, Parkinson's disease and hospital admissions: Frequencies, diagnoses and costs, Acta Neurologica Scandinavica. 121(1) (2010) 38-43.	Did not report number admitted for what reason
36.	B. Kelly, C. Blake, O. Lennon, Acute Hospital Admissions of Individuals with a Known Parkinson's Disease Diagnosis in Ireland 2009-2012: A Short Report. Journal of Parkinson Disease Print. 6(4) (2016) 709-716.	Did not report number admitted for what reason
37.	U. Lertxundi, A. Isla, M.A. Solinis, S.D. Echaburu, R. Hernandez, J. Peral-Aguirregoitia, J. Medrano, J.C. Garcia-Monco, Medication errors in Parkinson's disease inpatients in the Basque Country. Parkinsonism & Related Disorders, 36 (2017) 57-62.	Did not report number admitted for what reason
38.	H. Woodford, R. Walker, Emergency hospital admissions in idiopathic Parkinson's disease. Movement Disorders, 2005. 20(9): p. 1104-1108.	Did not report number admitted for what reason
39.	L. Shahgholi, S. De Jesus, S.S. Wu, Q.L. Pei, A. Hassan, M.J. Armstrong, D. Martinez-Ramirez, P. Schmidt, M.S. Okun, Hospitalization and rehospitalization in Parkinson disease patients: Data from the National Parkinson Foundation Centers of Excellence, Plos One. 12(7) (2017) 10.	Did not report number admitted for what reason
40.	M. Harris, M. Fry, The utilisation of one district hospital emergency department by people with Parkinson's disease, Australasian Emergency Nursing Journal. 20(1) (2017) 1-5.	Did not report number admitted for what reason
41.	J.A Temlett, P.D. Thompson, Reasons for admission to hospital for Parkinson's disease. Internal Medicine Journal. 36(8) (2006) 524-526.	Did not report number admitted for what reason
42.	A. Merola, R.P. Sawyer, C.A. Artusi, R. Suri, Z. Berndt, J.R. Lopez-Castellanos, J. Vaughan, J.A. Vizcarra, A. Romagnolo, A.J. Espay, J.R. Lopez-Castellanos, Orthostatic hypotension in Parkinson disease: Impact on health care utilization. Parkinsonism & Related Disorders. 47 (2018) 45-49.	Did not report number admitted for what reason
43.	A. Mahajan, P. Balakrishnan, A. Patel, I. Konstantinidis, D. Nistal, N. Annapureddy, P. Poojary, G.N. Nadkarni, C. Sidiropoulos, Epidemiology of inpatient stay in Parkinson's disease in the United States: Insights from the Nationwide Inpatient Sample, Journal of Clinical Neuroscience. 31 (2016) 162-5.	Did not report number admitted for what reason

44.	R. Gil-Prieto, R. Pascual-Garcia, J. San-Roman-Montero, P. Martinez-Martin, J. Castrodeza-Sanz, A. Gil-de-Miguel, Measuring the Burden of Hospitalization in Patients with Parkinson's Disease in Spain, PLoS ONE [Electronic Resource]. 11(3) (2016) e0151563.	Did not report number admitted for what reason
45.	D. Martinez-Ramirez, L. Almeida, J.C. Giugni, B. Ahmed, M. Higuchi, C.S. Little, J.P. Chapman, C. Mignacca, A.W. Shukla, C.W. Hess, K.W. Hegland, M.S. Okun, Rate of aspiration pneumonia in hospitalized Parkinson's disease patients: a cross-sectional study. Bmc Neurology. 15 (2015) 6.	Did not report number admitted for what reason
46.	V. Low, Y. Ben-Shlomo, E. Coward, S. Fletcher, R. Walker, C.E. Clarke, 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. 21(5) (2015) 449-54.	Did not report number admitted for what reason
47.	E.D. Louis, C. Henchcliffe, B.T. Bateman, C. Schumacher, Young-onset Parkinson's disease: hospital utilization and medical comorbidity in a nationwide survey, Neuroepidemiology. 29(1-2) (2007) 39-43.	Did not report number admitted for what reason
48.	O.H.H. Gerlach, M.P.G. Broen, P.H.M.F. van Domburg, A.J. Vermeij, W.E.J. Weber, Deterioration of Parkinson's disease during hospitalization: Survey of 684 patients. BMC Neurology. (2012) 13.	Did not report number admitted for what reason
49.	A.W. Willis, M. Schootman, R. Tran, N. Kung, B.A. Evanoff, J.S. Perlmutter, B.A. Racette, A.W. Willis, M. Schootman, R. Tran, N. Kung, B.A. Evanoff, J.S. Perlmutter, B.A. Racette, Neurologist-associated reduction in PD-related hospitalizations and health care expenditures, Neurology. 79(17) (2012) 1774-1780.	Did not report number admitted for what reason
50.	K.L. Chou, J. Zamudio, P. Schmidt, C.C. Price, S.A. Parashos, B.R. Bloem, K.E. Lyons, C.W. Christine, R. Pahwa, I. Bodis-Wollner, W.H. Oertel, O. Suchowersky, M.J. Aminoff, I.A. Malaty, J.H. Friedman, M.S. Okun, K.L. Chou, J. Zamudio, P. Schmidt, and C.C. Price, Hospitalization in Parkinson disease: a survey of National Parkinson Foundation Centers. Parkinsonism & Related Disorders. 17(6) (2011) 440-445.	Did not report number admitted for what reason
51.	M.Cosentino, E. Martignoni, D. Michielotto, D. Calandrella, G. Riboldazzi, C. Pacchetti, G. Frigo, G. Nappi, S. Lecchini, Medical healthcare use in Parkinson's disease: survey in a cohort of ambulatory patients in Italy. BMC Health Services Research. 5(1) (2005) 26.	Did not report number admitted for what reason
52.	R.W. Walker, J. Palmer, J. Stancliffe, B.H. Wood, A. Hand, W.K. Gray, Experience of care home residents with Parkinson's disease: Reason for admission and service use,	Did not report number

	Geriatrics & gerontology international. 14(4) (2014) 947-53.	admitted for what reason
53.	C.P. Derry, K.J. Shah, L. Caie, C.E. Counsell, Medication management in people with Parkinson's disease during surgical admissions, Postgraduate Medical Journal. 86(1016) (2010) 334-337.	Did not report number admitted for what reason
54.	J. Martins, A. Rua, N.V. Cha, Hospital Mortality in Parkinson's Disease: Retrospective Analysis in a Portuguese Tertiary Centre, Acta Medica Portuguesa. 29(5) (2016) 315-318.	Did not report number admitted for what reason
55.	S. Muzerengi, , C. Rick, I. Begaj, N. Ives, F. Evison, R.L. Woolley, C.E. Clarke, Coding accuracy for Parkinson's disease hospital admissions: implications for healthcare planning in the UK. Public Health. 146 (2017) 4-9.	Did not report number admitted for what reason
56.	P. Hobson, S. Roberts, G. Davies, The introduction of a Parkinson's disease email alert system to allow for early specialist team review of inpatients, BMC Health Services Research. 19(1) (2019) 271.	Did not report number admitted for what reason

Supplementary material, table 3: Reasons for admission

Study	Paul BS	Lubomski	Braga et	Skelly et	Klein et	Guneysel	Matignoni	Tan et	Kessler et
Reasons for	et	et	al	al(2014)	al(2009)	et al	et al(2004)	al(1998)	al(1972)
hospitalization	al(2017)	al(2014)	(2014)			(2008)			
Falls & fractures	+	+	+		+	+	+	+	
Infections	+	+	+	+	+	+	+	+	
(UTI &									
Pneumonia)									
Motor	+	+		+	+		+	+	+
complications									
CVS co-	+	+	+			+	+	+	
morbidities									
Neuropsychiatric	+	+	+		+		+	+	+
problems									
CVD/Stroke	+	+	+		+	+	+		
	•		•			·			
GIT problems	+	+	+		+	+	+	+	+
Genito-urinary	+		+				+	+	+
problems									
Neoplasia		+	+				+	+	
·									
Surgical							+	+	
problems									

Supplementary material, table 3 (contd): Reasons for admission

Study Reasons for hospitalization	Paul BS et al(2017)	Lubomski et al(2014)	Braga et al (2014)	Skelly et al(2014)	Klein et al(2009)	Guneysel et al(2008)	Matignoni et al(2004)	Tan et al(1998)	Kessler et al(1972)
Encephalo- pathy (delirium & electrolyte imbalance)	+	+	+		+	+			+
Dementia		+			+			+	
Syncope/ Orthostatic Hypotension		+	+	+	+		+		+
Other neurological problems	+		+		+				
Others (unmentioned)	+		+	+	+				

⁺ reported reason

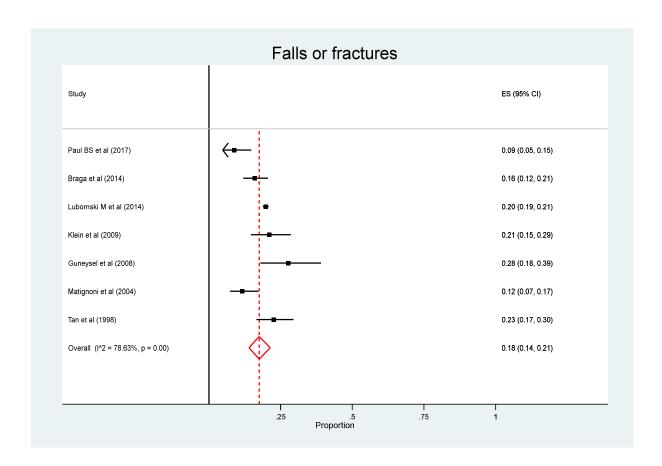
Supplementary material, Appendix 2: Results of Meta-analysis (pooled prevalence of common reasons for admission and study bias of the articles)

1. Falls/Fractures

Study	ES.	[95% Conf.	Interval]	
Paul BS et al (2017) Braga et al (2014) Lubomski M et al (20 Klein et al (2009) Guneysel et al (2008	0.16 0.20 0.21	0.12 0.19 0.15	0.21	
Matignoni et al (200 Tan et al (1998)				

Heterogeneity chi^2 = 28.08 (d.f. = 6) p = 0.00 I^2 (variation in ES attributable to heterogeneity) = 78.63% Estimate of between-study variance Tau^2 = 0.01

Test of ES=0 : z= 15.98 p = 0.00



Egger's test for small-study effects: Regress standard normal deviate of intervention effect estimate against its standard error

Number of studies = 7

Root MSE = .8303

Std_Eff	Coef.	Std. Err.	t	P> t	[95% Conf.	Interval]
slope bias	.2013329 3423053	.0143125	14.07 -0.78		.1645413 -1.476595	.2381244

Test of H0: no small-study effects P = 0.473

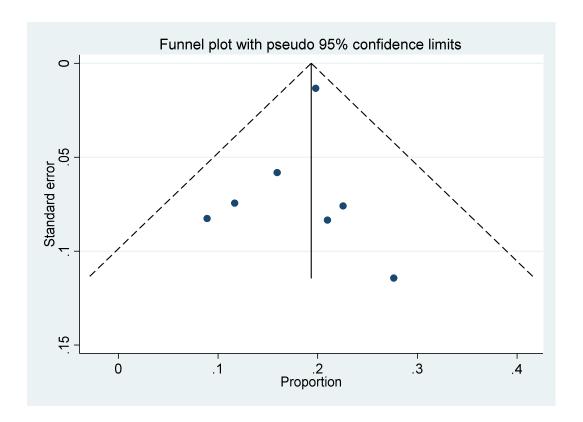
. metabias _ES _seES, beg

Note: data input format theta se_theta assumed.

Begg's test for small-study effects:

Rank correlation between standardized intervention effect and its standard err > or

adj. Kendall's Score (P-Q) = -1 Std. Dev. of Score = 6.66 Number of Studies = 7 z = -0.15 Pr > |z| = 0.881 z = 0.00 (continuity corrected) Pr > |z| = 1.000 (continuity corrected)

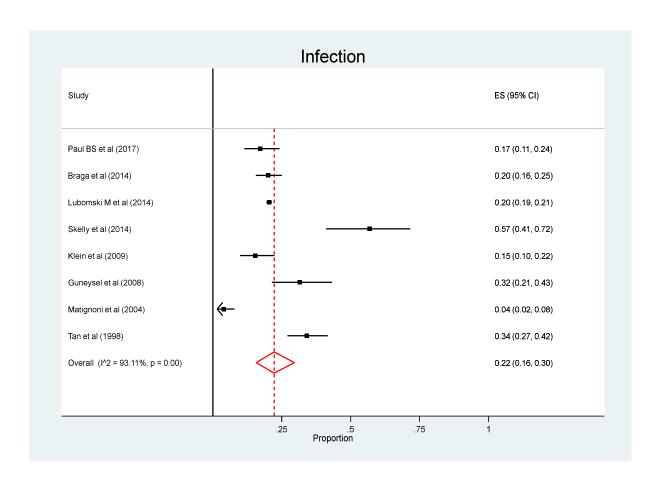


2. Infections (UTI & Pneumonia)

Study	ES.	_	_	
Paul BS et al (2017)	0.17	0.13	0.24	
Braga et al (2014)	0.20	0.16	6 0.25	
Lubomski M et al (20	0.20	0.19	0.21	
Skelly et al (2014)	0.57	0.43	1 0.72	
Klein et al (2009)	0.15	0.10	0.22	
Guneysel et al (2008	0.32	0.23	1 0.43	
Matignoni et al (200	0.04	0.02	2 0.08	
Tan et al (1998)	•			
Random pooled ES				

Heterogeneity chi^2 = 101.61 (d.f. = 7) p = 0.00 I^2 (variation in ES attributable to heterogeneity) = 93.11% Estimate of between-study variance Tau^2 = 0.05

Test of ES=0 : z= 10.68 p = 0.00



Egger's test for small-study effects: Regress standard normal deviate of intervention effect estimate against its standard error

Number of studies = 8 Root MSE = 1.57

Std_Eff	Coef.	Std. Err.	t	P> t	[95% Conf.	Interval]
slope bias	.1946493	.0263049		0.000	.1302834 -1.437925	.2590152

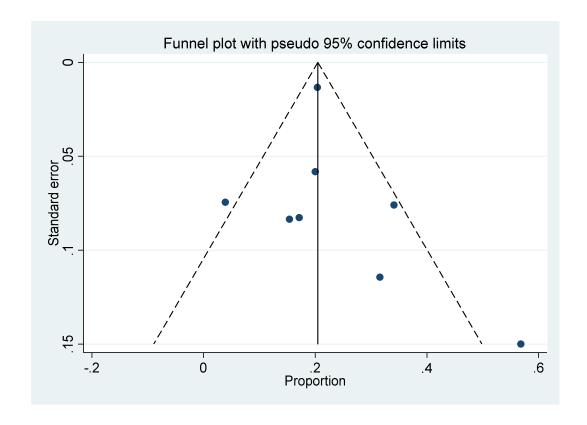
Test of H0: no small-study effects P = 0.597

. metabias _ES _seES, beg

Note: data input format theta se_theta assumed.

Begg's test for small-study effects:

Rank correlation between standardized intervention effect and its standard err > or

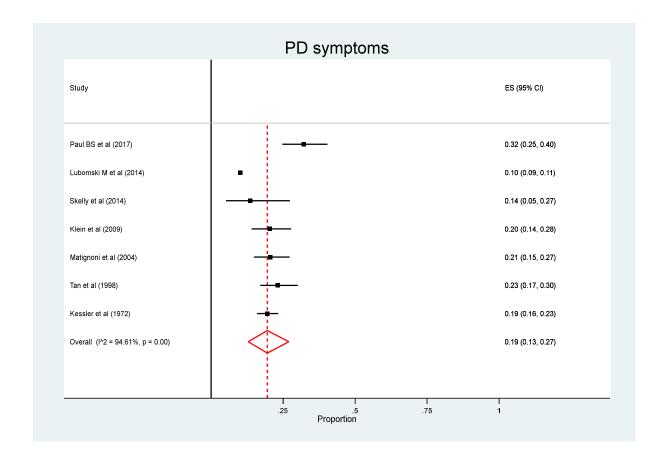


3. Worsening motor symptoms of PD

-	1	[95% Conf. Inter	-	
Paul BS et al (2017) Lubomski M et al (20	0.32	0.25	0.40	
Skelly et al (2014)			0.27	
Klein et al (2009)	0.20	0.14	0.28	
Matignoni et al (200	0.21	0.15	0.27	
Tan et al (1998)	0.23	0.17	0.30	
Kessler et al (1972)	'		0.23	
Random pooled ES	0.19	0.13	0.27	

Heterogeneity chi^2 = 111.22 (d.f. = 6) p = 0.00 I^2 (variation in ES attributable to heterogeneity) = 94.61% Estimate of between-study variance Tau^2 = 0.05

Test of ES=0 : z= 9.23 p = 0.00



Egger's test for small-study effects: Regress standard normal deviate of intervention effect estimate against its standard error

Number of studies = 7

Std_Eff	Coef.	Std. Err.	t	P> t	[95% Conf.	Interval]
slope bias	.0802673 1.780277	.0152701		0.003 0.013	.0410141	.1195204

Root MSE = .8907

Test of H0: no small-study effects P = 0.013

. metabias $_{ES}$ $_{seES}$, beg

Note: data input format theta se_theta assumed.

Begg's test for small-study effects:

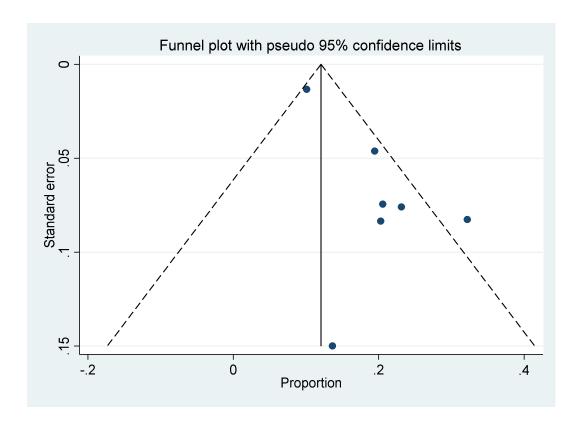
Rank correlation between standardized intervention effect and its standard err > or

adj. Kendall's Score (P-Q) = -1 Std. Dev. of Score = 6.66 Number of Studies = 7 z = -0.15 Pr > |z| = 0.881

z = 0.00 (continuity corrected)

Pr > |z| = 1.000 (continuity corrected)

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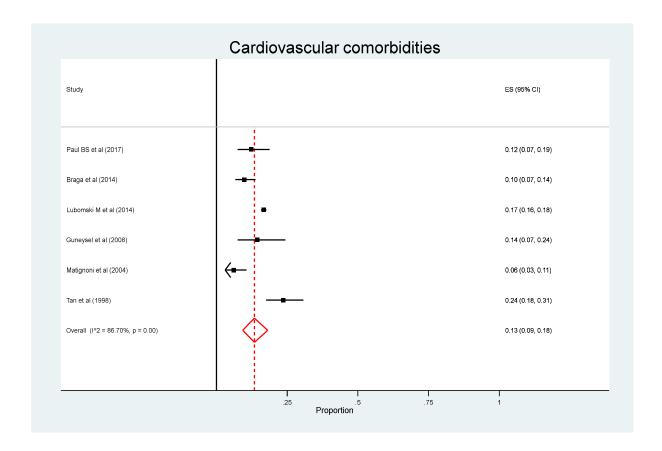
4. Cardiovascular co-morbidities

-	•	[95% Conf. I	_	
Paul BS et al (2017) Braga et al (2014)	0.12	0.07 0.07	0.19 0.14	
Lubomski M et al (20 Guneysel et al (2008 Matignoni et al (200	0.14	0.16 0.07 0.03	0.18 0.24 0.11	
Tan et al (1998)				
Random pooled ES		0.09		

Heterogeneity chi^2 = 37.60 (d.f. = 5) p = 0.00 I^2 (variation in ES attributable to heterogeneity) = 86.70% Estimate of between-study variance Tau^2 = 0.02

Test of ES=0 : z= 10.41 p = 0.00

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Egger's test for small-study effects: Regress standard normal deviate of intervention effect estimate against its standard error

Number of studies = 6

Std_Eff	Coef.	Std. Err.	t	P> t	[95% Conf.	Interval]
slope bias	.1732593 5475014		10.58 -1.02		.1278071 -2.044667	.2187116

Root MSE

.9341

Test of H0: no small-study effects P = 0.367

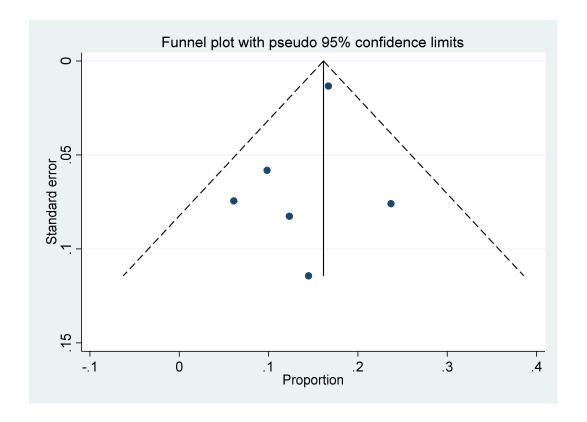
. metabias _ES _seES, beg

Note: data input format theta se_theta assumed.

Begg's test for small-study effects:

Rank correlation between standardized intervention effect and its standard err > or

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adj. Kendall's Score (P-Q) = -1 Std. Dev. of Score = 5.32 Number of Studies = 6 z = -0.19 Pr > |z| = 0.851 z = 0.00 (continuity corrected) Pr > |z| = 1.000 (continuity corrected)
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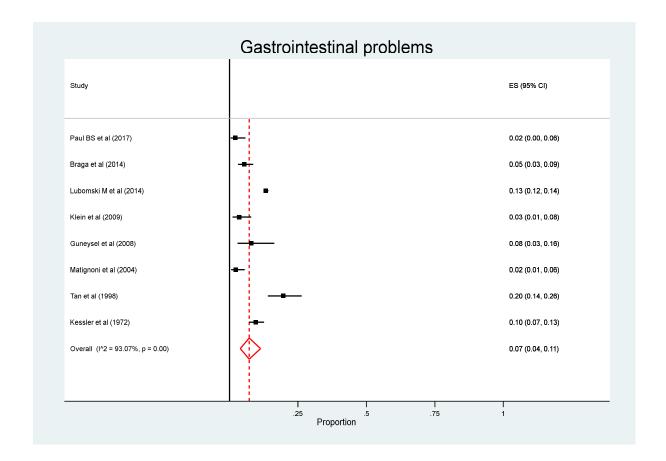


5. Gastrointestinal problems

Study	ES	_	Interval]	
Paul BS et al (2017)			0.06	
Braga et al (2014)	0.05	0.03	0.09	
Lubomski M et al (20	0.13	0.12	2 0.14	
Klein et al (2009)	0.03	0.03	0.08	
Guneysel et al (2008	0.08	0.03	0.16	
Matignoni et al (200	0.02	0.03	0.06	
Tan et al (1998)	0.20	0.1	0.26	
Kessler et al (1972)	1			
Random pooled ES	0.07	0.04	4 0.11	

Heterogeneity chi^2 = 100.95 (d.f. = 7) p = 0.00 I^2 (variation in ES attributable to heterogeneity) = 93.07% Estimate of between-study variance Tau^2 = 0.04

Test of ES=0 : z= 6.67 p = 0.00



Egger's test for small-study effects: Regress standard normal deviate of intervention effect estimate against its standard error

Number of studies = 8

Std_Eff	Coef.	Std. Err.	t	P> t	[95% Conf.	Interval]
slope bias		.0142487			.1103836 -2.033304	.1801144

Root MSE = .8266

Test of H0: no small-study effects P = 0.058

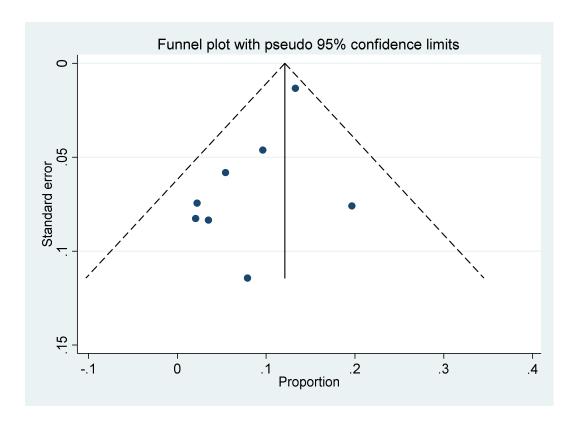
. metabias _ES _seES, beg

Note: data input format theta se_theta assumed.

Begg's test for small-study effects:

Rank correlation between standardized intervention effect and its standard err > or

adj. Kendall's Score (P-Q) = -4 Std. Dev. of Score = 8.08 Number of Studies = 8 z = -0.49 Pr > |z| = 0.621 z = 0.37 (continuity corrected) Pr > |z| = 0.711 (continuity corrected)

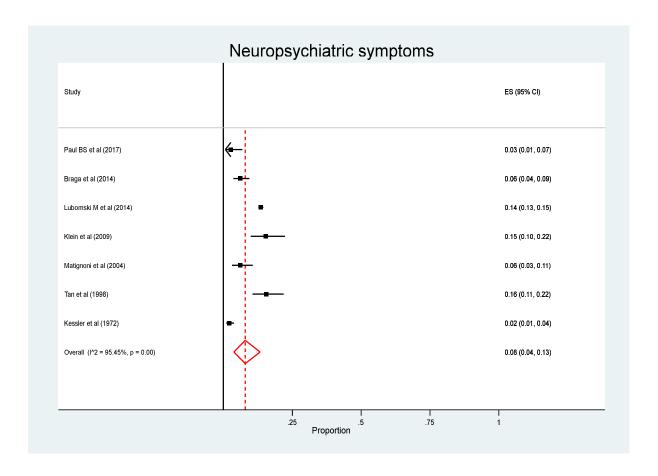


6. Neuropsychiatric complications

Study	_	95% Conf. Inter	-	
Paul BS et al (2017) Braga et al (2014) Lubomski M et al (20	0.03 0.06 0.14	0.01 0.04 0.13	0.07 0.09 0.15	
Klein et al (2009) Matignoni et al (200 Tan et al (1998)	0.06		0.22 0.11 0.22	
Kessler et al (1972)	' 			

Heterogeneity chi^2 = 131.81 (d.f. = 6) p = 0.00 I^2 (variation in ES attributable to heterogeneity) = 95.45% Estimate of between-study variance Tau^2 = 0.05

Test of ES=0 : z= 5.77 p = 0.00



Egger's test for small-study effects: Regress standard normal deviate of intervention effect estimate against its standard error

Number of studies = 7 Root MSE = 1.08

Std_Eff	Coef.	Std. Err.	t	P> t	[95% Conf.	Interval]
slope bias	.1461752 -1.042285	.0191666	7.63 -1.71		.0969059 -2.605371	.1954444

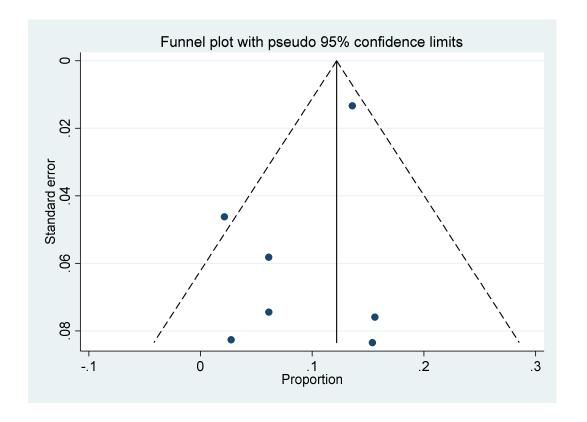
Test of H0: no small-study effects P = 0.147

. metabias _ES _seES, beg

Note: data input format theta se_theta assumed.

Begg's test for small-study effects:

Rank correlation between standardized intervention effect and its standard err > or



Supplementary material: General characteristics excluded papers which provided no data for analysis but had reasons for admissn

Author	Year	Country	Study design	Aim of study	Main reasons for admission reported
Hobson et al	2019	United Kingdom	Retrospective	Describe method, introduction and economic costs of introducing an e-alert system for PD specialist team for PwPD* attending ED.	Falls/fractures, UTI, feeling unwell, medication problems.
Merola et al	2018	USA	Retrospective	Evaluate the effect of orthostatic hypotension on health care utilization among PwPD	Falls, neuropsychiatric complications and Rehabilitation
Shahgholi et al	2017	USA	Prospective	To evaluate hospital admissions and identify associated factors.	Infections, cardiovascular and respiratory co-morbidities, cancer.
Muzerengi et al	2017	United Kingdom	Retrospective	To estimate the number of PD admissions to a large Birmingham hospital and assess the coding accuracy.	Infections, falls, fractures, cardiovascular and circulatory disorders.
Lertxundi et al	2017	Spain	Retrospective	To evaluate the prevalence of medication errors.	PD-related complications, UTI, Pneumonia
Harris M et al	2017	Australia	Retrospective	To describe trends and characteristics of older PwPD presenting to ED.	Falls, pain, infection and general review.
Martins J et al	2016	Portugal	Retrospective	To identify inpatient mortality (reasons for hospital admission and cause of death) in PwPD admitted to a tertiary hospital.	Pneumonia, sepsis from UTI, Stroke, End-stage cancer
Mahajan et al	2016	USA	Retrospective	To confirm that care on a specialist in-patient PD Unit (SPDU) would improve outcomes of urgent medical care among PwPD.	Pneumonia, UTI, Sepsis, Aspiration pneumonitis, Rehabilitation, CCF.

Supplementary material:General characteristics excluded papers which provided no data for analysis but had reasons for admissn

Author	Year	Country	Study design	Aim of study	Main reasons for admission reported
Kelly B et al	2016	Republic of Ireland	Retrospective	To outline preventable admissions among PwPD in order to inform primary care initiatives that will help maintain their health status.	Respiratory diseases-Pneumonia, Pneumonitis due to swallowing problems, COPD, UTI, Fracture.
Gil-Prieto et al	2016	Spain	Retrospective	To estimate the incidence of hospitalizations among PwPD from 1997 to 2012 in Spain.	Infections and parasitic diseases, Neoplasms, Endocrine, nutritional, metabolic.
Martinez et al	2015	USA	Retrospective	To evaluate the frequency of aspiration events in PwPD during hospital encounters.	Fall/fractures, Pulmonary, general medical and gastrointestinal problems.
Low et al	2015	United Kingdom	Retrospective	To determine the magnitude and direct healthcare costs and reasons for admission and mortality among PwPD in order to recommend preventive initiatives to reduce hospitalizations.	PD related problems, UTI, Pneumonia, Septicaemia, cellulitis, Delirium, Syncope, Orthostatic hypotension.
Walker et al	2014	United Kingdom	Retrospective	To establish the needs of care home residents with PD.	Falls, confusion, decreased mobility, fractures, UTI, Swallowing problems, Pneumonia.
Guttman M et al	2004	Turkey	Retrospective	To evaluate the diagnosis most responsible for hospitalization in a large cohort of patients with Parkinsonism.	PD related symptoms, Pneumonia, cardiovascular, cerebrovascular and GIT disorders.
				•	

Supplementary material:General characteristics excluded papers which provided no data for analysis but had reasons for admissn

Author	Year	Country	Study design	Aim of study	Main reasons for admission reported
Willis A et al	2012	USA	Retrospective	To establish that greater familiarity with neurologic disease gained specialty training would lead to a reduction in PD related morbidity and improvement in outcomes.	PD-related problems: neurodegenerative disease, psychosis, UTI
Gerlach O et al	2013	The Netherlands	Prospective	To analyse prospectively whether or not there is deterioration of motor function at discharge of hospitalized PwPD compared to admission, and if so, assess its severity and related factors.	Orthopaedic reviews: Hip fracture and hip replacement surgery; Neurology: PD medication errors, worsening PD symptoms;.
Chou K et al	2011	USA	Prospective	To explore current practises and opinions at National Parkinson foundation centres regarding hospitalization of PwPD.	Elective surgery, falls/fractures, Infections, aspiration pneumonia, medication issues
Vossius C et al	2010	Norway	Prospective	To give an estimate on the incremental economic impact of hospitalization in PD to the society.	Cardiovascular disorders, Pneumonia, cancer, trauma, genitourinary tract disorders.
Derry C et et al	2010	United Kingdom	Retrospective	To examine the pharmacological management of PwPD during surgical admissions.	Missed doses of medication, orthopaedic surgeries for fractures

Supplementary material:General characteristics excluded papers which provided no data for analysis but had reasons for admissn

Author	Year	Country	Study design	Aim of study	Main reasons for admission reported
Louis E et al	2007	USA	Retrospective	To use a large administrative database to compare hospital utilization and outcomes among people with young onset PD and controls.	UTI, pneumonia, rehabilitation, psychosis, fractures.
Temlett M et al	2006	Australia	Retrospective	To compare the number of admissions related to management of primary motor disorder with the number admitted for secondary problems such as falls, cognitive disorders, drug side-effects and the complications of immobility.	Fractures/falls, Pneumonia, cardiovascular, GIT and urinary disorders, motor fluctuations and dyskinesias, confirm diagnosis and levodopa responsiveness.
Woodford H et al	2005	United Kingdom	Retrospective	To try and understand for which patients, and what reasons, emergency admission is required.	Infective disease, pneumonia, UTI, cardiovascular disorders, falls, decreased mobility/dyskinesia, fractures, orthostatic hypotension.
Consentino M et al		Italy	Retrospective	To assess the reasons for medical healthcare use among PwPD and determine the relationship between health care use and pattern of antiparkinsonian drug medications.	Rehabilitation, chest pain, fractures, falls, pneumonia, dyskinesias, dysphagia.

^{*}People with Parkinson's Disease