Journal of Parkinsonism and Restless Legs Syndrome

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Prevalence of depression and receipt of antidepressant pharmacotherapy among patients with Parkinson's disease: a national assessment of US office-based physician visits

This article was published in the following Dove Press journal:
Journal of Parkinsonism and Restless Legs Syndrome
16 November 2017
Number of times this article has been viewed

Nicole K Early
Alyssa M Peckham
Kathleen A Fairman
David A Sclar

Department of Pharmacy Practice, Midwestern University College of Pharmacy – Glendale, Glendale, AZ, USA

Background: The prevalence of comorbid depression in patients with Parkinson's disease (PD) is estimated to range from 17% to 25%, although up to 35% to 42% of patients with PD display clinically significant depressive symptoms. Untreated depression leads to a worsening course of PD, decreased quality of life, and increased mortality.

Methods: Data were obtained from the US National Ambulatory Medical Care Survey (NAMCS) of office-based physician visits made in 2013 and 2014. For office visits with a diagnosis of PD (International Classification of Diseases, 9th Revision [ICD-9] code 332.0), the study measures included the rates of diagnosed depression (ICD-9 codes 296.2, 296.3, 300.4, or 311), recording of depression as a comorbidity, and prescribing of antidepressant pharmacotherapy. Analytic results were compared with those of a similar study that measured depression diagnosis (ICD-9 codes) and antidepressant prescribing, using NAMCS data for 1990–1995.

Results: In 2013–2014, 29.8% of patients with PD were provided ≥1 antidepressant for any indication, triple the rate that was observed in 1990–1995 (8.6%). From 1990–1995 to 2013–2014, the percentage of patients with an ICD-9 code for comorbid depression increased from 4.1% to 8.3%, and the percentage with both an ICD-9 code and antidepressant pharmacotherapy increased from 3.2% to 7.2%. Of patients with an ICD-9 code for depression, 78.2% in 1990–1995 and 87.1% in 2013–2014 were prescribed antidepressant medication. In 2013–2014, 14.8% of patients with PD had recognized depression, measured by either ICD-9 code or NAMCS comorbidity indicator.

Conclusion: In office-based physician visits made by US patients with PD, the rate of antidepressant prescribing for diagnosed depression more than doubled from 1990–1995 to 2013–2014. However, the 14.8% prevalence of recognized depression remains lower than that suggested by previous studies of PD. Further research is needed to assess the reasons for these findings and promote optimal physical and mental health among patients with PD.

Keywords: Parkinson's disease, depression, antidepressant, National Ambulatory Medical Care Survey

Correspondence: Nicole K Early
Department of Pharmacy Practice, Midwestern University College of Pharmacy – Glendale, 19555 North 59th Avenue, Glendale, AZ 85308, USA
Tel +1 623 572 3544
Fax +1 623 572 3550
Email nearly@midwestern.edu

Introduction

Parkinson's disease (PD) is a chronic, progressive neurodegenerative disorder,[1] affecting nearly 1% of persons aged ≥60 years and up to 4% of those older than 80 years.[2] These prevalence rates are expected to increase in the future because of worldwide improvements in life expectancy.[2] In addition to tremor, debilitating nonmotor symptoms of

PD – including sleep disorders, dementia, and dysfunction of the autonomic nervous system – have a profoundly negative effect on quality of life.[3]

In patients with a diagnosis of PD, the prevalence of depression is estimated to range from 17% to 25%, although up to 35%–42% of patients with PD display clinically significant depressive symptoms regardless of official depression diagnosis.[4,5] Despite the known association of PD with depression,[6] accurate assessment of comorbid depression in patients with PD can be difficult for several reasons.[3,7] These include overlapping disease symptomatology, variations in depression diagnostic criteria, and availability of multiple assessment tools and techniques.[3,7] For example, one prospective study found that clinicians diagnosed depression in 21% of patients with PD; however, per standardized testing, ~44% screened positive for depression.[3] This finding suggests that depression may be detected in less than one-half of symptomatic patients.[3]

Untreated and undertreated depression in PD can lead to worsening motor function,[8,9] hastened cognitive decline,[8,10] decreased quality of life,[11] and increased mortality.[12] In addition, nonmotor features of PD, such as depression, may lead to significant disability despite improvement in motor symptoms.[13] Thus, it is essential that symptoms of depression be promptly recognized and adequately addressed to prevent an expedited course of PD deterioration, in an effort to improve quality of life of patients and caregivers.[8,11]

Depression in patients with PD is often treated with antidepressants, usually selective serotonin reuptake inhibitors (SSRIs) because of their favorable side effect profile in the elderly.[14] Historically, there has been concern that antidepressants could worsen motor function given the serotonergic inhibition of dopaminergic firing.[14] However, recent data have shown that antidepressant use in PD has rendered motor impairment either unchanged[15–19] or significantly improved,[20] as measured by the motor portion of the Unified Parkinson's Disease Rating Scale.

A previous study by Sclar et al, which assessed US physician office-based care provided to patients with PD from 1990 to 1995, found that depression was diagnosed in only 4.1% of physician office visits.[21] In addition, only 3.2% of visits made by patients with PD from 1990 to 1995 included both depression diagnosis and prescribing of antidepressant pharmacotherapy.[21] Since then, published guidelines have emphasized the importance of screening for nonmotor disorders, including depression, in patients with PD.[13] The present study was conducted to update the 1990–1995 findings, using a similar data set, sample, and analytic methodology, to provide current estimates of the prevalence of depression and the use of antidepressant pharmacotherapy in US office-based physician visits.

Methods

Study data were derived from the National Ambulatory Medical Care Survey (NAMCS), a nationally representative, cross-sectional survey of US office-based physician visits that has been conducted annually by the National Center for Health Statistics since 1973.[22–24] Survey data, which are collected by the US Bureau of the Census and available as public-use data files, include patient demographics, diagnoses, and comorbidities; services and treatments provided or ordered during the visit; and prescribed medications.[24] NAMCS data are publicly available and widely used as a source for numerous assessments of medical care and prescribed medications in ambulatory settings in the US, including studies of psychiatric disorders and treatments.[25–33]

The survey uses a stratified probability sampling procedure comprising multiple stages: first, selection by geographic area (eg, counties or county groups); second, within each geographic area by physician name, stratified by physician specialty; and third, by week, with each sampled physician randomly assigned to 1 of 52 weeks of data collection each year.[22,23] Finally, from each physician and week, a sample of office visits is chosen at random.[22,23] In 2014, the most recent year for which NAMCS data were publicly available as of the initiation of the present study, the rate of survey response by physician offices was 54.8%.[34]

Because the NAMCS is designed to represent office-based physician visits, the sample excludes administrative contacts, such as telephone calls and medication refills.[22] Weights provided in the NAMCS data file for each recorded office visit can be applied to the data to yield nationally representative estimates, adjusting for the complex sampling design and for nonresponse.[35]

The sample for the present study included all physician office visits made in 2013 or 2014 by patients aged ≥20 years with a diagnosis of PD, defined as an International Classification of Diseases, 9th Revision (ICD-9) diagnosis code of 332.0 in primary, secondary, or tertiary diagnosis fields. This sampling methodology was the same as that used by Sclar et al to assess physician office visits made by patients with PD in 1990–1995.[21]

To identify patients with depression, two definitions were used. The first was based on ICD-9 code and measured whether the patient had a diagnosis of 296.2x (major depressive disorder, single episode); 296.3x (major depressive

disorder, recurrent episode); 300.4 dysthymic disorder); or 311 (depressive disorder, not elsewhere classified), in any of the aforementioned three diagnosis fields. The second was based on comorbidities recorded for the office visit in response to a survey item that read: "Regardless of the diagnoses written above, does the patient now have…" accompanied by a list of potential comorbid conditions, including depression.[34,36]

Treatments measured for the visit included 1) the provision or ordering of a depression screening examination and (2) the prescribing of antidepressant pharmacotherapy, measured using Multum category 249. This Multum category includes SSRIs, serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants, tetracyclic antidepressants, monoamine oxidase inhibitors, and other antidepressant medications.[34,36]

Statistical analyses were descriptive because after weighting, the large sample size represents all office visits provided in the US.[22,23,35] All analyses were performed using SPSS version 23.0 (IBM Corporation, Armonk, NY, USA).

Results

From 2013to 2014, more than 3 million office-based physician visits were made by US patients with PD, more than 90% of whom were aged ≥60 years, and 52.5% of whom were male (Table 1). Medicare covered approximately two-thirds of the visits, whereas private insurance covered 28.7%. Neurologists provided the majority (58.1%) of care, with general/family practitioners providing 12.1% and internal medicine specialists another 12.7%.

Antidepressant medications (for any indication) were prescribed in 29.8% of visits made by patients with PD in 2013–2014, a rate more than triple the 8.6% identified by Sclar et al for visits made by patients with PD in 1990–1995 (Table 2).[21] The rate of diagnosed depression more than doubled from 4.1% in 1990–1995 to 8.3% in 2013–2014. Depression was recognized, either diagnosed or recorded as a comorbidity, for 14.8% of patients in 2013–2014.

Within the 2013–2014 sample, 7.2% of patients were both diagnosed with depression and prescribed antidepressant pharmacotherapy; and 12.2% had depression, measured by either diagnosis or comorbidity indicator, and were prescribed antidepressant pharmacotherapy (Table 2). Of patients with diagnosed depression, 78.2% in 1990–1995 and 87.1% in 2013–2014 were prescribed antidepressant pharmacotherapy. Of those with recognized depression (ie, either diagnosis or comorbidity indication) in 2013–2014, 82.3% were prescribed antidepressant pharmacotherapy.

Table 1 Characteristics of patients aged ≥20 years with a diagnosis of Parkinson's disease: US office-based physician visits in 2013–2014

Characteristics	N	%
Total unweighted, n	174	–
Total weighted, n	3,180,324	100.0
Patient characteristics		
Age group (years)		
≤50	26,396	0.8
50–59	272,873	8.6
60–69	1,106,290	34.8
70–79	969,743	30.5
≥80	805,023	25.3
Sex		
Female	1,509,593	47.5
Male	1,670,732	52.5
Race/ethnicity		
White non-Hispanic	2,000,883	62.9
Black non-Hispanic	360,880	11.3
Hispanic	774,923	24.4
Other	43,639	1.4
Payment source		
Private insurance	791,308	28.7
Medicare	1,804,954	65.4
Medicaid	5,829	0.2
Other	157,719	5.0
Comorbidities		
Cerebrovascular disease	122,263	3.8
Chronic kidney disease or ESRD	26,887	0.8
Congestive heart failure	54,522	1.7
Hyperlipidemia	458,118	14.4
Hypertension	992,332	31.2
Heart disease: CAD, IHD, or previous MI	121,553	3.8
Physician specialty		
General or family practice	385,925	12.1
Internal medicine	403,363	12.7
Psychiatry	73,683	2.3
Neurology	1,847,256	58.1
Other	470,097	14.8
Seen by primary care physician	760,194	24.3

Note: Parkinson's disease is defined as ICD-9-CM code 332.0x in the primary, secondary, or tertiary diagnosis fields.

Abbreviations: CAD, coronary artery disease; ESRD, end-stage renal disease; ICD-9, International Classification of Diseases, 9th Revision; IHD, ischemic heart disease; MI, myocardial infarction.

Discussion

This analysis of publicly available US NAMCS data on office-based physician visits produced two key findings about prevalence of, and treatment for, depression in patients with PD. First, the rate of recognized comorbid depression in patients with PD is 8.3% when measured by diagnosis only and 14.8% when both diagnoses and comorbidity indicators are assessed. Second, the percentage of patients with PD who were prescribed an antidepressant for any reason more than tripled from 1990–1995 to 2013–2014, although

Table 2 Depression screening and treatment provided to patients aged ≥20 years with a diagnosis of Parkinson's disease: US office-based physician visits in 1990–1995 versus 2013–2014

Characteristic	1990–1995[a] (%)	2013–2014 (%)
Prescribed an antidepressant[b]	8.6	29.8
Screened for depression[c]	NA	5.6
Depression diagnosed[d]	4.1	8.3
And prescribed an antidepressant[b]	3.2	7.2
Prescribed an antidepressant, as a proportion of those diagnosed	78.2	87.1
Depression diagnosed[d] and/or indicated in record[e]	NA	14.8
And prescribed an antidepressant[b]	NA	12.2
Prescribed an antidepressant, as a proportion of those with depression diagnosed or indicated in record	NA	82.3

Notes: [a]Data from Sclar et al, 1998.[21] [b]SSRIs, SNRIs, tricyclic antidepressants, tetracyclic antidepressants, MAOIs, and any other antidepressant medication recorded as Multum category 249. [c]Reflects whether patient was screened for depressive disorder. [d]Defined as ICD-9 codes of 296.2x (major depressive disorder, single episode), 296.3x (major depressive disorder, recurrent episode), 300.4 (dysthymic disorder), or 311 (depressive disorder, not elsewhere classified). [e]Refers to a section of the questionnaire that asked: "Regardless of the diagnoses previously entered, does the patient now have…". NA, not available because the item was not available in 1990–1995 or was not reported in the article by Sclar et al.[21]

Abbreviations: ICD-9, International Classification of Diseases, 9th Revision; MAOI, monoamine oxidase inhibitor; SNRI, selective norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

the proportion of patients with diagnosed depression who received antidepressant medication increased modestly – from 78% to 87% – during that time period.[21]

While interpreting these findings, it should be noted that both the number of marketed antidepressants and the number of US Food and Drug Administration-approved and off-label indications have markedly increased in the past two decades. From 1995 to 2014, ~15 new molecular entities and formulations of antidepressants were added to the US prescription market.[37] New indications for antidepressant pharmacotherapy include primarily anxiety disorders, such as generalized anxiety disorder, obsessive-compulsive disorder, panic disorder, posttraumatic stress disorder, and social anxiety disorder.[38] Anxiety disorders occur in up to 40% of patients with PD.[39] This rate is significantly greater than that of the general population of older adults, which is estimated to range from 3.2% to 14.2%.[39] Other common on- and off-label indications for antidepressant treatment include, but are not limited to, bipolar depression, peripheral neuropathy, smoking cessation, insomnia, fibromyalgia, musculoskeletal pain, migraines, and various eating disorders.[38,40]

In addition to the increase in all-cause antidepressant use, the present study found more than twofold increases in diagnosis of depression (from 4.1% to 8.3%) and in diagnosis of depression plus antidepressant pharmacotherapy (from 3.2% to 7.2%) in office visits made by patients with PD, comparing 1990–1995 with 2013–2014.[21] This shift in increased recognition and treatment could be the result of practice guidelines promulgated by the American Academy of Neurology in 2006,[13] which suggest that nonmotor symptoms of PD, such as depression, can lead to significant disability.

The diagnosis of depression in PD is challenging due to overlap in symptoms and a multifaceted pathophysiology.[14,41] Depression should be suspected in patients with PD who experience a rapid decline in function over a short time period of days to weeks.[41] In addition to effects on motor symptoms, it is reasonable to suggest that modification of dopaminergic therapy may result in the improvement of nonmotor symptoms;[42] however, evidence about whether enhanced pharmacologic management of PD improves depressive symptoms is inconsistent.[4,10,13,42–44]

Limitations

First, the NAMCS is a sample of office visits to community-based physicians and therefore does not capture care delivered in inpatient or outpatient hospitals.[22] Second, NAMCS documents diagnostic codes based upon a practitioner's clinical evaluation of the patient. Subjective clinical opinion may lead to lack of uniformity and consistency when entering diagnostic codes.[6] Third, the NAMCS does not measure patient history or the severity of comorbidities recorded in the medical record.[22,34,36] It is possible that patients with milder depression had been screened and/or diagnosed at an earlier visit and were being treated with psychotherapy rather than pharmacotherapy at the time of the office visit recorded in the NAMCS database. However, the NAMCS records medications that are either newly prescribed or continued, so the rate of pharmacotherapy measured in the present study reflects the current medication treatment status as of the date of the office visit.[34,36]

Conclusion

From 1990–1995 to 2013–2014, the percentage of patients with PD who were prescribed an antidepressant for any reason more than tripled and the rate of diagnosed comorbid depression more than doubled in US office-based physician visits. Among patients with diagnosed depression, most patients in both the time periods were treated with antidepressant pharmacotherapy. However, given previous estimates that up to 35%–42% of patients with PD display clinically significant depressive symptoms, the 15% rate of recognized depression observed in the present study suggests that depression may remain under-recognized in patients with PD. Further

research is needed to identify and assess the reasons for these findings, thereby informing efforts to promote optimal physical and mental health among patients with PD.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Suchowersky O, Reich S, Perimutter J, et al. Practice parameter: diagnosis and prognosis of new onset Parkinson disease (an evidence-based review). *Neurology*. 2006;66(7):968–975.
2. De Lau LML, Breteler MMB. Epidemiology of Parkinson's disease. *Lancet Neurol*. 2006;5(6):525–535.
3. Reijnders JSAM, Ehrt U, Weber WEJ, Aarsland D, Leentjens AF. A systematic review of prevalence studies of depression in Parkinson's disease. *Mov Disord*. 2008;23(2):183–189.
4. Slaughter JR, Slaughter KA, Nichols D, Holmes SE, Martens MP. Prevalence, clinical manifestations, etiology, and treatment of depression in Parkinson's disease. *J Neuropsychiatry Clin Neurosci*. 2001;13(2):187–196.
5. Hsu YT, Liao CC, Chang SN, et al. Increased risk of depression in patients with Parkinson disease: a nationwide cohort study. *Am J Geriat Psychiatry*. 2015;23(9):934–940.
6. Veazey C, Aki SO, Cook KF, Lai EC, Kunik ME. Prevalence and treatment of depression in Parkinson's disease. *J Neuropsychiatry Clin Neurosci*. 2005;17(3):310–323.
7. Shulman LM, Taback RL, Rabinstein AA, Weiner WJ. Non-recognition of depression and other non-motor symptoms in Parkinson's disease. *Parkinsonism Relat Disord*. 2002;8(3):193–197.
8. Ng A, Chander RJ, Tan LC, Kandiah N. Influence of depression in mild Parkinson's disease on longitudinal motor and cognitive function. *Parkinsonism Relat Disord*. 2015;21(9):1056–1060.
9. Ravina B, Camiciolo R, Como PG, et al. The impact of depressive symptoms in early Parkinson disease. *Neurology*. 2007;69(4):342–347.
10. Starkstein SE, Mayberg HS, Leiguarda R, Preziosi TJ, Robinson RG. A prospective longitudinal study of depression, cognitive decline, and physical impairments in patients with Parkinson's disease. *J Neurol Neurosurg Psychiatry*. 1992;55(5):377–382.
11. Müller B, Assmus J, Herlofson, Larsen JP, Tysnes OB. Importance of motor vs. non-motor symptoms for health-related quality of life in early Parkinson's disease. *Parkinsonism Relat Disord*. 2013;19(11):1027–1032.
12. Hughes TA, Ross HF, Mindham RH, Spokes EG. Mortality in Parkinson's disease and its association with dementia and depression. *Acta Neurol Scand*. 2004;110(2):118–123.
13. Miyasaki JM, Shannon K, Voon V, et al. Practice parameter: evaluation and treatment of depression, psychosis, and dementia in Parkinson disease (an evidence-based review). *Neurology*. 2006;66:996–1002.
14. Leo RJ. Movement disorders associated with the serotonin selective reuptake inhibitors. *J Clin Psychiatry*. 1996;57(10):449–454.
15. Marino S, Sessa E, Di Lorenzo G, et al. Sertraline in the treatment of depressive disorders in patients with Parkinson's disease. *Neurol Sci*. 2008;29:391–395.
16. Antonini A, Tesei S, Zecchinelli A, et al. Randomized study of sertraline and low-dose amitriptyline in patients with Parkinson's disease and depression: effect on quality of life. *Mov Disord*. 2006;21:1119–1122.
17. Avila A, Cardona X, Martin-Baranera M, Maho P, Sastre F, Bello J. Does nefazodone improve both depression and Parkinson disease? A pilot randomized trial. *J Clin Psychopharmacol*. 2003;23:509–513.
18. Dell'Angello G. SSRIs do not worsen Parkinson's disease: evidence form an open label, prospective study. *Clin Neuropharmacol*. 2001;24:221–227.
19. Ceravolo R, Nuti A, Piccinni A, et al. Paroxetine in Parkinson's disease: effects on motor and depressive symptoms. *Neurology*. 2000;55:1216–1218.
20. Rampello L, Chiechio S, Raffaele R, Vecchio I, Nicoletti F. The SSRI, citalopram, improves bradykinesia in patients with Parkinson's disease treated with L-dopa. *Clin Neuropharmacol*. 2002;25:21–24.
21. Sclar DA, Robison LM, Skaer TL, Galin RS. Depression in Parkinson's disease: a national survey of office-based visits 1990-1995. *Int J Geriatr Psychopharmacol*. 1998;1:216–219.
22. U.S. Centers for Disease Control and Prevention, National Center for Health Statistics. Ambulatory health care data: NAMCS scope and sample design [updated 2010 January 15]. Available from: https://www.cdc.gov/nchs/ahcd/ahcd_scope.htm. Accessed July 27, 2017.
23. U.S. Centers for Disease Control and Prevention, National Center for Health Statistics. NAMCS data collection and processing [updated 2011 August 15]. Available from: https://www.cdc.gov/nchs/ahcd/ahcd_data_collection.htm. Accessed July 27, 2017.
24. U.S. Centers for Disease Control and Prevention, National Center for Health Statistics. Questionnaires, datasets, and related documentation. Public-use data files (1973-2015) [updated August 31, 2017]. Available from: https://www.cdc.gov/nchs/ahcd/ahcd_questionnaires.htm. Accessed September 18, 2017.
25. Barnett ML, Linder JA, Clark CR, Sommers BD. Low-value medical services in the safety-net population. *JAMA Intern Med*. 2017;177(6):829–837.
26. Mafi JN, Wee CC, Davis RB, Landon BE. Association of primary care practice location and ownership with the provision of low-value care in the United States. *JAMA Intern Med*. 2017;177(6):838–845.
27. Mojtabai R. Does depression screening have an effect on the diagnosis and treatment of mood disorders in general medical settings? An instrumental variable analysis of the National Ambulatory Medical Care Survey. *Med Care Res Rev*. 2011;68(4):462–489.
28. Swanoski MT, Little MM, St Hill CA, Ware KB, Chapman S, Lutfiyya MN. Potentially inappropriate medication prescribing in U.S. older adults with selected chronic conditions. *Consult Pharm*. 2017;32(9):525–534.
29. Gerlach LB, Olfson M, Kales HC, Maust DT. Opioids and other central nervous system-active polypharmacy in older adults in the United States. *J Am Geriatr Soc*. 2017;65(9):2052–2056.
30. Akincigil A, Matthews EB. National rates and patterns of depression screening in primary care: results from 2012 and 2013. *Psychiatr Serv*. 2017;68(7):660–666.
31. Patel SR, Humensky JL, Olfson M, Simpson HB, Myers R, Dixon LB. Treatment of obsessive-compulsive disorder in a nationwide survey of office-based physician practice. *Psychiatr Serv*. 2014;65(5):681–684.
32. Gerhard T, Akincigil A, Correll CU, Foglio NJ, Crystal S, Olfson M. National trends in second-generation antipsychotic augmentation for nonpsychotic depression. *J Clin Psychiatry*. 2014;75(5):490–497.
33. Rege S, Sura S, Aparasu RR. Atypical antipsychotic prescribing in patients with depression. *Res Social Adm Pharm*. 2017 Epub Aug 2.
34. U.S. Centers for Disease Control and Prevention, National Center for Health Statistics. 2014 NAMCS micro-data file documentation. Available from: ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/NAMCS/doc2014.pdf. Accessed July 28, 2017.
35. U.S. Centers for Disease Control and Prevention, National Center for Health Statistics. NAMCS estimation procedures [updated November 6, 2015]. Available from: https://www.cdc.gov/nchs/ahcd/ahcd_estimation_procedures.htm. Accessed September 18, 2017.
36. U.S. Centers for Disease Control and Prevention, National Center for Health Statistics. 2013 NAMCS micro-data file documentation. Available from: ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/NAMCS/doc2013.pdf. Accessed September 18, 2017.
37. Center Watch. FDA Approved Drugs for Psychiatry/Psychology. Available from: https://www.centerwatch.com/drug-information/fda-approved-drugs/therapeutic-area/17/psychiatry-psychology. Accessed July 3, 2017.

38. U.S. Centers for Medicare & Medicaid Services, Medicaid Integrity Group. Antidepressant medications: use in adults. August 2013. Available from: https://www.cms.gov/Medicare-Medicaid-Coordination/Fraud-Prevention/Medicaid-Integrity-Education/Pharmacy-Education-Materials/Downloads/ad-adult-factsheet.pdf. Accessed September 18, 2017.
39. Pontone GM, Williams JR, Anderson KE, et al. Pharmacologic treatment of anxiety disorders in Parkinson's disease. *Am J Geriatr Psychiatry.* 2013;21(6):520–526.
40. Wong J, Motulsky A, Abrahamowicz M, et al. Off-label indications for antidepressants in primary care: descriptive study of prescriptions from an indication based electronic prescribing system. *BMJ*. 2017;356:j603.
41. Rickards H. Depression in neurological disorders: Parkinson's disease, multiple sclerosis, and stroke. *J Neurol Neurosurg Psychiatry.* 2005;76 (Suppl 1):i48–i52.
42. Barone P, Scarzella L, Marconi R, et al. Pramipexole versus sertraline in the treatment of depression in Parkinson's disease: a national multicenter parallel-group randomized study. *J Neurol.* 2006;253:601–607.
43. March GG, Markham CH. Does levodopa alter depression and psychopathology in Parkinsonism patients? *J Neurol Neurosurg Psychiatry.* 1973;36:925–935.
44. Choi C, Sohn YH, Lee JH, Kim J. The effect of long-term levodopa therapy on depression level in de novo patients with Parkinson's disease. *J Neurol Sci.* 2000;172:12–16.