Movement Disorders
CLINICAL PRACTICE
RESEARCH ARTICLE

Prevalence and Correlates of Anti-Parkinson Drug Use in a Nationally Representative Sample

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Abstract: **Background:** Although numerous prescription drugs are available to treat Parkinson's disease (PD), little is known about national use in clinical practice and which factors may influence variability in care. The objectives of this study were to describe the prevalence of anti-Parkinson drug use among Medicare beneficiaries with PD and to identify demographic and clinical factors associated with drug use.
Methods: This retrospective study was based on a random sample of annual 5% Medicare Part A and B claims linked with Medicare Part D drug files from 2007 through 2010. The study sample included fee-for-service Medicare beneficiaries with continuous stand-alone Part D enrollment who had been diagnosed with PD in the given year. First, any PD drug use and drug use by class (levodopa, dopamine agonist, anticholinerigc, monoamine oxidase B inhibitors, catechol-O-methyltransferase inhibitors, and amantadine) were described. Using generalized estimating equation regressions, patient and provider characteristics associated with anti-Parkinson drug use and choice were examined.
Results: Over 81% of patients with PD were treated with anti-Parkinson drugs, and this proportion was stable over the 4 years of the study. The majority were treated with levodopa (90%); followed by dopamine agonists (29–31%); then monoamine oxidase B inhibitors, anticholinergics, amantadine, and catechol-O-methyltransferase inhibitors (all between 5% and 11%). Holding all else equal, patients who were not seen by a neurologist (odds ratio, 0.41; 95% confidence interval, 0.38–0.44; $P < 0.001$) and African-American patients (odds ratio, 0.80; 95% confidence interval, 0.69–0.93; $P = 0.003$) were significantly less likely to be treated.
Conclusions: Among a national sample of Medicare beneficiaries with PD, the majority received anti-Parkinson drugs. However, there was relative under-treatment of African-Americans and patients who were not seen by a neurologist for care.

Parkinson's disease (PD) affects at least 1 million people in the United States and increases both their morbidity and their mortality.[1] However, effective symptomatic treatment exists. Under-utilization of appropriate pharmacologic treatment is associated with greater disability, decreased survival, and lowered health-related quality of life.[2]

Evidence-based reviews of PD management recommend treatment with levodopa (L-dopa), dopamine agonists, monoamine oxidase B (MAOB) inhibitors, catechol-O-methyltransferase inhibitors (COMTIs), and amantadine to improve clinical outcomes.[3–6] However, with incident disease, only from one-third to two-thirds of patients with PD start therapy.[7–9] In those with moderate to advanced disease, while most patients should be on anti-Parkinson drugs, medication management varies widely, and there is no clear consensus on the optimal regimen.

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The choice and utilization of anti-Parkinson drugs may vary for numerous reasons unrelated to clinical factors. Researchers have documented that patient characteristics, such as race and socioeconomic status, are independently associated with treatment differences in numerous conditions.[10] There is preliminary evidence that this may be true in PD as well.[8] Provider characteristics, such as specialty type, may also contribute to the choice and use of anti-Parkinson drugs. Care provided by neurologists for PD is associated with improved survival compared with primary care providers; however, women and minorities are less likely to be seen by neurologists.[11] It remains unknown whether at least some differences in health outcomes are attributable to different patterns of medications prescribed to patients.

In 2006, the US government introduced Medicare Part D, which is the prescription drug benefit program to increase access to prescription drugs for adults over the age of 65 years and for those who are severely disabled. However, little has been published about the prevalence and correlates of anti-Parkinson drug use in this population, which has the highest prevalence of PD.[12] The purpose of this study was to estimate the prevalence of anti-Parkinson drug use and choice among Medicare beneficiaries and to identify patient and provider characteristics associated with drug use and choice in order to elucidate potential mechanisms of high-quality care and disparities in treatment.

Patients and Methods

Study Design, Data Source, and Sample

This was a retrospective analysis of prevalent cases of PD using annual cross-sections of Medicare beneficiaries from 2007 to 2010. Medicare is a US government-financed health insurance program for the elderly and disabled. It supports the care of 98% of Americans older than 65 years of age. The data source for the study was the 5% Medicare Chronic Condition Warehouse, which includes Medicare inpatient, outpatient, and carrier claims files; Medicare Part D prescription drug-event and plan characteristics files; and a personal summary file with demographic and enrollment information for a 5% random sample of Medicare beneficiaries. The study sample included fee-for-service Medicare beneficiaries who had at least 12 months of continuous, stand-alone Part D enrollment and a diagnosis of PD in the given year. To be considered a PD case, beneficiaries must have had at least 1 Medicare-reimbursed inpatient claim (as either the primary or secondary diagnosis) or 2 outpatient claims (physician visits only) for PD (International Classification of Diseases, 9th Revision [ICD-9], code 332.0). We excluded individuals who were enrolled in a health maintenance organization due to incomplete data availability. There was no requirement that these claims had to be separated by a minimum time frame. This method optimizes sensitivity (range, 64–89%) over specificity (range, 28–99%) based on prior studies that have evaluated the diagnostic accuracy of administrative claims compared with the gold standard of either self-reported diagnoses or review of clinical information.[13–16] However, to further improve the specificity of our case definition, and to decrease the risk of misclassification of secondary parkinsonian syndromes in our cohort, we also excluded individuals with a history of schizophrenia (ICD 295) or secondary/atypical parkinsonism (ICD codes 332.1 and 333.X). Similar case ascertainment methods have been used in previous health care utilization studies of Medicare populations.[11,12]

Dependent Variables

First, we examined the use of any anti-Parkinson drug in each year. We defined any anti-Parkinson drug use as having 1 or more prescription claims for at least 1 PD medication for greater than 30 days. Only anti-Parkinson drugs approved by the US Food and Drug Administration for the treatment of PD were included. Next, we categorized anti-Parkinson drug use into the following classes: (1) L-dopa, (2) dopamine agonists, (3) anticholinergics, (4) MAOB inhibitors, (5) COMTIs, and (6) amantadine. Finally, we counted the number of unique anti-Parkinson drugs (individual agents) that were used per year by each patient.

Independent Variables

Patient characteristics, including age, sex, race and ethnicity, Part D low-income subsidy status, and county of residence, were abstracted from the Medicare files. We extrapolated measures of county-level socioeconomic status, such as education, income, and unemployment, from the Area Resource File. County-level estimates of neurologist availability (the number of neurologists per 100,000 nondisabled Medicare beneficiaries) were generated using Medicare physician data and beneficiary summary file data. Measures of PD-related comorbidities that could affect PD medication utilization and/or choice were recorded based on ICD-9 codes for dementia, anxiety, depression, psychosis/hallucinations, falls, fractures, leg edema, orthostatic hypotension and syncope, and deep brain stimulation implantation. In addition, the burden of overall non-PD–related comorbidity was measured using the prescription drug hierarchical condition category (RxHCC) risk score. This risk score is created using the Center for Medicare and Medicaid Services' RxHCC model, which is designed to determine payment for prescription drugs under Part D and is based on the presence of 197 medical conditions recorded on Medicare diagnostic claims.[17] Finally, the specialty of the treating provider was abstracted based on Medicare provider specialty codes and was categorized as neurologist or nonneurologist.

Statistical Analysis

The prevalence of any anti-Parkinson drug use and the number of unique anti-Parkinson drugs used were described individually and according to different drug classes. Generalized estimating equation logistic regression models were used to account for

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clustering of patients across multiple years and to estimate the adjusted association between patient and provider characteristics and the following variables: (1) any anti-Parkinson drug use, (2) the number of unique PD drugs used (ordinal logistic regression), and (3) the type of anti-Parkinson drug class used. Bonferroni correction was used to adjust for the multiple comparisons made across the 6 different regression models of anti-Parkinson drug class.[18] A $P < 0.0083$ was used as the threshold for statistical significance. Coefficients are reported as odds ratios (OR) with 95% confidence intervals (CIs) and 2-sided P values. All analyses were performed using the SAS software package (SAS Institute, Inc., Cary, NC).

Ethics

The Institutional Review Board at the University of Pennsylvania approved the study protocol with a waiver of written informed consent.

Results

For the years from 2007 through 2010, the sample sizes ranged from 9482 to 9626 individuals. This represents a random sample from almost 200,000 Medicare beneficiaries with PD in standalone Part D plans in each year. Table 1 describes the sample according to demographic and clinical characteristics for each annual cohort. The majority of patients with PD were white (range, 87.2–88.1%), and African Americans represented from 5.3% to 5.8% of the cohort. Approximately 60% of all patients were seen by neurologists during the year.

The majority of PD patients (range, 81–82%) were prescribed at least 1 anti-Parkinson drug each year. On average, individuals with PD were on from 1.55 to 1.59 unique anti-Parkinson drugs. Figure 1 shows the proportion of patients who were on 1, 2, 3, 4, or ≥5 unique anti-Parkinson drugs. Of the treated patients, 90% were on L-dopa therapy. This was followed by therapy with dopamine agonists (29–31%), MAOB inhibitors

TABLE 1 Demographic and clinical characteristics of patients with Parkinson's disease from a 5% Medicare sample, 2007–2010

Characteristic	Year			
	2007	2008	2009	2010
Sample size, no.	9482	9626	9566	9503
Demographics				
Age, %				
<65 y	5.3	5.0	5.4	5.9
65–69 y	7.8	7.7	7.8	8.3
70–74 y	13.9	14.5	14.6	13.9
75–79 y	19.8	19.5	19.3	20.1
80–84 y	24.5	24.8	23.7	23.2
>85 y	28.7	28.5	29.1	28.7
Sex: Men, %	39.0	39.5	40.3	41.6
Race, %				
White	88.1	88.1	87.7	87.2
African-American	5.6	5.3	5.4	5.8
Hispanic	2.7	2.6	2.9	2.8
Other	3.7	4.0	4.0	4.2
Low-income subsidy (LIS), %				
Full	45.6	44.2	43.8	43.5
Partial	0.9	0.9	0.9	0.9
Non-LIS	50.4	52.1	52.4	52.9
County-level socioeconomic status measures				
Education: less than high school, %	14.3	13.9	13.9	13.9
Median income, US$	34,921	36,665	36,574	37,352
Unemployment, %	4.8	5.9	9.4	9.7
County-level measure of access to neurologists				
No. of neurologists in county per 100,000 population	69.8	70.0	69.6	71.9
PD-related comorbidity, %				
Anxiety	16.7	18.6	19.8	20.0
Depression	30.5	32.4	32.4	32.9
Psychosis or hallucinations	18.9	19.0	19.4	19.0
Dementia	11.2	12.2	12.9	13.2
Falls	5.8	6.0	9.8	10.9
Fractures	9.3	8.5	8.4	7.7
Deep brain stimulation	1.3	1.3	1.8	2.0
Leg edema	18.8	19.2	19.8	20.7
Orthostatic hypotension	11.7	12.1	12.0	12.9
Syncope	12.1	12.6	12.2	12.5
Other comorbidities				
RxHcc, mean	1.19	1.22	1.22	1.24
Measure of specialty care				
Sees neurologist, %	58.8	60.3	60.5	61.7

PD, Parkinson's disease; RxHcc, prescription drug hierarchical condition category.

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(9–11%), amantadine (7–8%), COMTIs (6–8%), and anticholinergics (5–6%) (Table 2).

In multivariate regression analyses controlling for patient demographics, county-level socioeconomic status measures, specialty data, overall and PD-related comorbidity, being seen by a neurologist for care (OR, 2.42; 95% CI, 2.26–2.60) was significantly associated with an increased odds of anti-Parkinson drug use, whereas greater overall comorbidity was associated with a decreased odds of anti-Parkinson drug use (OR, 0.54; 95% CI, 0.50–0.59). Being seen by a neurologist also was significantly associated with being treated with multiple anti-Parkinson drugs (OR, 2.40; 95% CI, 2.33–2.57), and greater overall comorbidity was associated with a decreased odds of treatment with multiple anti-Parkinson drugs (OR, 0.52; 95% CI, 0.49–0.57). Overall, younger patients were more likely to be on multiple PD medications compared with older patients. In addition, nonclinical factors, including African-American race (with white race as the reference category; OR, 0.80; 95% CI, 0.69–0.93), and partial low-income subsidy (with full low-income subsidy as the reference category; OR, 0.61; 95% CI, 0.44–0.85), were associated with a significantly decreased odds of any anti-Parkinson drug use. African-American race was also associated with decreased odds of being on multiple anti-Parkinson drugs compared with whites (OR, 0.69; 95% CI, 0.59–0.80). Although there was no significant association between sex and any anti-Parkinson drug use (OR, 1.03; 95% CI, 0.95–1.10), among those who were treated, women were significantly less likely to be on multiple anti-Parkinson drugs (OR, 0.91; 95% CI, 0.85–0.98) (Table 3).

In a multivariate examination of specific drug class choice (Table S1), older age groups were associated with greater odds of being on L-dopa and lower odds of receiving a dopamine agonist, an MAOB inhibitor, amantadine, or anticholinergic therapy. Patients with PD who were seen by a neurologist were significantly more likely to be on dopamine agonists, MAOB inhibitors, amantadine, or COMTIs, but not L-dopa or anticholinergics. African Americans were significantly less likely to be treated with dopamine agonists (OR, 0.68; 95% CI, 0.57–0.81) than whites. Women had a significantly lower odds of being on L-dopa (OR, 0.80; 95% CI, 0.71–0.89), MAOB inhibitors (OR, 0.76; 95% CI, 0.67–0.85,) and COMTIs (OR, 0.73; 95% CI, 0.64–0.84) than men.

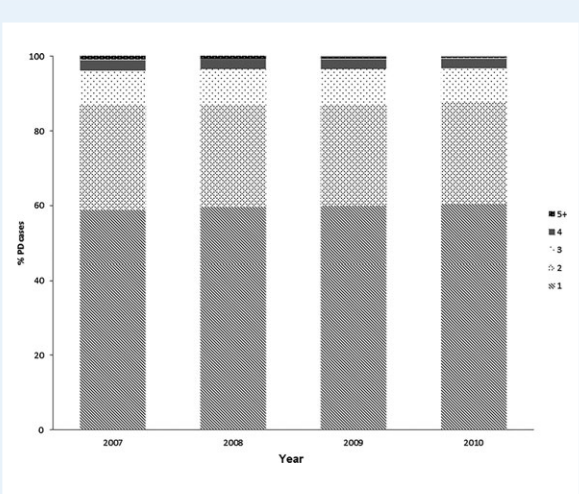

Figure 1 Distribution of the number of unique anti-Parkinson drugs used per year.

TABLE 2 Patterns of anti-Parkinson drug use and choice among Medicare beneficiaries, 2007–2010

Variable	Year			
	2007	2008	2009	2010
Total no. of patients with PD cases	9482	9626	9566	9503
No. of anti-Parkinson drug users	7721	7872	7835	7725
Use of any anti-Parkinson drug, %	81	82	82	81
Levodopa use, %	90	90	90	90
Dopamine agonist use, %	31	31	30	29
MAOB inhibitor use, %	9	9	10	11
Anticholinergic use, %	6	6	6	5
Amantadine use, %	8	7	7	7
COMT inhibitor use, %	8	7	7	6

PD, Parkinson's disease; MAOB, monoamine oxidase-B; COMT, catechol-O-methyltransferase.

Discussion

In a nationally representative sample of Medicare beneficiaries, most patients with PD were treated with anti-Parkinson drugs, and the overwhelming majority was on L-dopa. Overall, this reflects a cost-sensitive and effective approach to treatment. However, several groups were identified that were vulnerable to disparate treatment: African Americans, women, and patients who were not seen by a neurologist. This suggests that there may be potential areas for continued improvement in the pharmacological management of patients with PD in clinical practice, as discussed below.

An older study that investigated the prevalence of anti-Parkinson drug use in the United States, but was limited only to nursing home residents, found that only 44% of patients with PD were treated.[19] A subsequent study using national survey data from the Medicare Current Beneficiary Survey (2000–2003) reported anti-Parkinson drug use at a higher rate of 58%, but this was still lower than our results.[20] However, the same study also noted that having prescription drug coverage was significantly associated with higher odds of anti-Parkinson drug use. Several years later, our results indicating that from 81% to 82% of patients were treated might reflect several factors. Implementation of the Medicare Part D prescription drug program in 2006 has resulted in greater utilization of standard therapies for many common disorders (such as heart failure and diabetes). It is likely that our results also reflect an increase in access to medications for the PD population. In addition, earlier suspicions that anti-Parkinson drug therapy might be harmful

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TABLE 3 Independent predictors of any anti-Parkinson drug use and the number of unique anti-Parkinson drugs used*

Covariate	Any anti-Parkinson drug use			Greater no. of unique anti-Parkinson drugs used		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Demographics						
Age, y						
65–69 (Ref)						
<65	0.81	0.68–0.97	0.025	1.20	1.02–1.41	0.029
70–74	1.09	0.94–1.26	0.261	0.84	0.75–0.95	0.004
75–79	1.05	0.91–1.22	0.467	0.70	0.63–0.79	<0.001
80–84	0.96	0.83–1.10	0.534	0.55	0.49–0.61	<0.001
≥85	0.88	0.77–1.0	0.078	0.40	0.36–0.45	<0.001
Women	1.03	0.95–1.10	0.500	0.91	0.85–0.98	0.008
Race						
White (Ref)						
African-American	0.80	0.69–0.93	0.003	0.69	0.59–0.80	<0.001
Hispanic	0.89	0.72–1.10	0.287	1.00	0.81–1.25	0.989
Other	1.11	0.92–1.35	0.280	1.32	1.10–1.58	0.003
Low-income subsidy (LIS)						
Full LIS (Ref)						
Non-LIS only	1.01	0.93–1.09	0.819	0.95	0.88–1.03	0.194
Partial LIS	0.61	0.44–0.85	0.003	0.75	0.53–1.05	0.090
Other comorbidities						
RxHcc	0.54	0.50–0.59	<0.001	0.53	0.49–0.57	<0.001
Measure of specialty care						
Sees neurologist	2.42	2.26–2.60	<0.001	2.40	2.23–2057	<0.001

*Models control for all variables listed and for county-level measures of socioeconomic status and access as well as PD-related comorbidity.
OR, odds ratio; CI, confidence interval; Ref, reference category; RxHcc, prescription drug hierarchical condition category.

are being refuted. There is now increasing scientific evidence that PD medication therapy, particularly L-dopa, is not toxic.[21] Thus, there is growing comfort with its prescription by providers and acceptance by patients.

Our finding that L-dopa is the most frequently prescribed anti-Parkinson drug aligns with several other studies in different samples. Among incident cases of PD in the United States, L-dopa is prescribed as initial therapy in greater than 70% of individuals.[22,23] In population-based studies in Italy and France, the results are similar[24,25]; and, in a sample of hospitalized patients with PD, 85% are treated with L-dopa.[26]

However, our study findings highlight that racial disparities in PD treatment remain pervasive. In a study of state Medicaid claims, African Americans with incident PD were significantly less likely to be started on medication therapy than whites.[8] Similarly, African-American nursing home residents with PD are less likely to receive anti-Parkinson drugs.[19] African Americans with PD are also less likely to receive therapeutic surgery,[27–29] receive appropriate management of comorbid depression,[30] or be represented in relevant clinical trials.[31] Our findings that African Americans are relatively undertreated for PD compared with whites is consistent with these earlier results. Although the prevalence and incidence of PD may be lower in those of African descent,[32] 1 study demonstrated that the response to standard therapy did not differ by race or ethnicity.[33] Furthermore, reports indicate that African Americans with treated PD have greater disability and disease severity when they present for care at PD centers compared with whites.[34,35] This prior evidence suggests that the need for anti-Parkinson drugs should be even greater among African Americans relative to whites. However, the extent to which our observed racial differences in treatment are due to clinical utility, physician preference/bias, or patient beliefs or adherence is unknown.

Women with PD were another group that experienced disparate treatment. They were less likely to be on multiple anti-Parkinson drugs or to receive L-dopa, MAOB, or COMTI therapy. This may reflect differences in clinical symptoms or response to medications. Overall, women with PD had fewer symptoms than men in 1 clinic-based study[36] although another report demonstrated that women had greater disability.[37] This could translate into different types and amounts of anti-Parkinson drug prescriptions; however, to our knowledge, there is no evidence that this practice results in improved health outcomes. In addition, there is some evidence that women with PD may be more likely to experience dyskinesias, although studies have been limited by small samples and multiple comparisons.[37,38] An increased risk of L-dopa–induced dyskinesias may be related to the reduced metabolism of L-dopa in individuals with lower body weight,[39] which, in turn, may explain the lower likelihood for women in this sample to be treated with L-dopa to limit side effects. Finally, it is possible that the disparate treatment observed is related to nonclinical factors, such as patient preference, physician bias, or other unmeasured socioeconomic confounders.

Another important finding from this study is that individuals with PD who were treated by a neurologist were significantly more likely to receive anti-Parkinson drug therapy as well as more complicated medication regimens. There is evidence that neurological care in PD is associated with improved health outcomes.[11] This raises the intriguing possibility that the improved outcomes seen with neurological care may be due at least in part to greater use of anti-Parkinson drugs. Similarly, a study of

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US veterans demonstrated that movement disorder specialists were significantly more likely to adhere to various quality indicators in the management of PD compared with general neurologists and nonneurologists.[40] These quality indicators included treatment of wearing-off and assessments of falls, depression, and hallucinations. It is important to understand the sources of variability in processes of care and outcomes between specialists and nonspecialists so that we can implement clinical pathways or practice guidelines to improve the quality of care for all PD patients.

There were several limitations of this study. First, we relied on administrative claims to identify patients with PD. This method could lead to misclassification errors due to (1) inaccurate PD diagnosis, (2) missing PD cases, and (3) coding errors.[16] Because our goal was to describe prescription drug utilization and patterns, we chose a PD case definition that optimized sensitivity first and then specificity. Prior studies have compared the accuracy of Medicare claims in the identification of PD; however, they employed slightly different methodologies.[13,15] Noyes and colleagues compared PD diagnosis by self-report ("Have you ever been told you have Parkinson's disease?") against physician-only claims for ICD code 332.0 and found that the highest positive predictive value was 74%. However, in a smaller sample (N = 28), Jain and colleagues compared physician review of medical records against any 2 Medicare claims and found a lower positive predictive value at 48% (95% CI, 0.30–0.68). It is possible that the inclusion of nonphysician claims in that prior study led to a greater false-positive rate. Taken together, it seems likely that there are still PD cases that are being missed when relying on diagnostic claims alone, which would lead to an underestimate of the number of detected cases of PD. It is also likely that cases identified as PD by their diagnostic code had another related condition (e.g., atypical or vascular parkinsonism) or no parkinsonism at all, which would bias our findings on the proportion of patients with PD who receive treatment. Furthermore, if misclassification of cases differed between groups (e.g., African Americans and whites), then it might confound observed differences. Also, the use of administrative data does not allow for the examination of more detailed clinical information, which could influence drug use and choice, such as motor disability or functional measures. However, we did control for possible PD-related comorbidities captured in the data set, such as comorbid dementia or psychosis, in an attempt to account for clinical differences that may affect treatment. It is also important to note that these data only capture prescription fills, not what a provider prescribed or what a patient actually consumed, although, claims for prescription fills are widely used and validated measures of drug use in the literature.

This study provides an important description of anti-Parkinson drug use among Medicare beneficiaries in real-world clinical practice at a national level. We find that a large majority of patients with PD, when provided prescription drug coverage under Medicare Part D, receive treatment. However, several areas for continued improvement and investigation still remain. The need for and response to PD treatment in women and minorities requires much additional study to develop effective strategies that will improve the appropriate adoption of PD therapy in these groups. In addition, increased access to neurological expertise for patients with PD may raise the number of treated individuals. Public policy strategies to improve access to expert PD care include adoption of telehealth consultations; increasing the supply of neurologists, particularly in underserved areas; and providing financial incentives for the provision of high-value, evidence-based care.

Author Roles

1. Research Project: A. Conception, B. Organization, C. Execution; 2. Statistical Analysis: A. Design, B. Execution, C. Review and Critique; 3. Manuscript Preparation: A. Writing the First Draft, B. Review and Critique.

N.D.: 1A, 1B, 1C, 2A, 2C, 3A
A.W.W.: 1A, 1B, 2C, 3B
P.L.: 1B, 1C, 2A, 2B, 3B
J.A.D.: 1B, 1C, 2A, 2B, 2C, 3B

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Disclosures

Ethical Compliance Statement: We confirm that we have read the Journal's position in issues involved in ethical publication and affirm that this work is consistent with those guidelines.

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Supporting Information

Additional Supporting Information may be found online in the supporting information tab for this article:

Table S1. Independent predictors of choice of drug class.

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