

Factors Predicting the Use of Multiple Psychotropic Medications

Michael B. Nichol, Ph.D., Glen L. Stimmel, Pharm.D.,
and Suk C. Lange, Pharm.D., M.P.H.

Background: Recent studies have questioned the appropriateness of some types of psychotropic medication prescribing, especially by general practitioners. The purpose of this study is to investigate factors that predict prescribing of multiple psychotropic medications, a class that may represent more complicated cases.

Method: This study analyzed data from the 1989 National Ambulatory Medical Care Survey (NAMCS). Multiple logistic regression methods were used to determine variables that predicted the provision or ordering of multiple psychotropic medications during a single office visit.

Results: Patients who visited psychiatrists were six times more likely to receive psychotropics in combination than patients visiting general practitioners. Patients diagnosed as manic were four times more likely to receive multiple psychotropics, and those diagnosed as schizophrenic were three times more likely. Patients visiting physicians in the Northeast and South were significantly less likely to receive psychotropics in combination than patients in the Midwest.

Conclusion: Although general practice physicians contribute to the use of multiple psychotropic medications, patients visiting psychiatric specialists are much more likely to be provided combination therapy.

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Reprint requests to: Michael B. Nichol, Ph.D., Department of Pharmaceutical Economics and Policy, USC School of Pharmacy, CHP-140F, 1540 East Alcazar Street, Los Angeles, CA 90033.

A number of health care researchers have noted that some psychotropic medication prescribing appears to be suboptimal, especially with regard to prescribing by primary care physicians.¹⁻³ The limited data presently available indicate that prescribers rarely note appropriate psychiatric diagnoses in conjunction with psychotropic use² and that medications used within particular categories (such as antidepressants) may have side effect profiles that negatively affect patient outcome.¹ Several authors have noted that primary care physicians represent a significant portion of the mental health network and prescribe the majority of psychotropic medications,^{2,4} although they may not have extensive training in the diagnosis and treatment of patients with mental diseases.

An area of prescribing that has not been investigated is the simultaneous use of multiple psychotropic medications. By definition, patients requiring multiple psychotropic medications can be considered complicated, and the potential for inappropriate therapy is high, if only because of the increased likelihood of adverse effects and drug interactions. Several problem areas may develop as a result of multiple concomitant psychotropic use: duplicative effects (two or more medications from the same class), offsetting effects (two or more medications that have opposite action), and lack of therapeutic indication (two or more medications in which there is inappropriate use). Multiple psychotropic prescribing with these characteristics has the potential to create significant negative patient outcomes.

There is increasing interest in the special problems of patients with co-occurring disorders.^{5,6} The lack of attention to multiple psychotropic prescribing is understandable since it occurs relatively infrequently and few data sources provide sufficient detail regarding drug use and diagnosis to determine inappropriate use categorically. However, concomitant use of psychotropics provides a distinct opportunity to identify physician and patient characteristics that may account for this lack of attention, especially insofar as it might be possible to determine whether primary care physicians contribute disproportionately to problem prescribing. The purpose of this research is threefold: to identify

the prevalence of multiple psychotropic prescribing by drug category, to classify potential inappropriate or questionable prescribing of multiple psychotropics, and to determine which factors predict multiple psychotropic prescribing behavior.

CONCEPTUAL BACKGROUND

One model that has been used extensively to predict the use of health services is that proposed by Andersen⁷ and expanded by Andersen and Newman⁸ in which health care decision making is hypothesized to be affected by four sets of variables: predisposing, enabling, need, and health services characteristics. Predisposing characteristics include such issues as family composition, social structure, and health beliefs. The enabling category includes family and community resources. The need category incorporates concepts of illness and patient response. This model has been employed to explain prescription and over-the-counter drug use⁹⁻¹¹ and a variety of other health services.¹²

The 1989 National Ambulatory Medical Care Survey (NAMCS) provides data on each of these four dimensions. For the purposes of this study, the predisposing factors included patient age, gender, and ethnicity. Patient age has been shown to be associated with increasing use of medications in a variety of studies.¹³⁻¹⁵ Women have been shown to be more likely to use prescriptions¹³ and are more likely to be prescribed psychotropic medications.^{16,17} Several authors^{18,19} have included ethnicity variables as covariates in studies of psychotropic medication use, but their results were conflicting. Therefore, the impact of ethnicity could not be predicted.

Enabling variables encompassed the specialty of the physician and the type of health insurance coverage used to pay for the patient visit. Physician specialty could be expected to be a good predictor of multiple psychotropic prescribing because more complicated mental health cases that may require multiple medications are likely to be supervised by psychiatrists. Evidence from the 1985 NAMCS established that psychiatrists prescribed multiple psychotropics more frequently than physicians in other specialties.¹ It can be expected that health maintenance organization (HMO) patients may receive less intensive care than those whose care is financed through fee-for-service insurance plans,²⁰ although treatment outcome appears to be comparable.²¹ Less intensive care may mean that patients are less likely to receive multiple prescriptions.

Need variables, for the purposes of this model, include whether the patient presented a psychiatric complaint, diagnostic categories identified by the physician, and whether the appointment was a repeat

visit for the same problem. Presence of a psychiatric complaint was used as an explanatory variable because it represents a clear indication that patient perception corresponds to prescribed medication, even though the complaint may also be expressed in terms of a physical manifestation of illness not easily connected to mental diagnoses.^{22,23} Diagnosis identified by the physician could be expected to be a strong predictor of drug prescribing, except for the fact that existing studies indicate that primary care physicians may not recognize psychiatric disorders³ or may be reluctant to identify mental health diagnoses.² The fact that the physician had previously treated the patient for a similar condition may be correlated with the use of multiple psychotropics, since a second visit for the same diagnosis could imply that the condition may be chronic or complicated.

Two variables were used to measure health system characteristics: region of the country and the provision of psychotherapy services. Extensive research has shown that health care service utilization varies dramatically throughout the United States.²⁴ Wells et al.²⁵ used Health Insurance Experiment data to show that residents living in sites in western and eastern states were more likely to visit mental health specialists than those in midwestern sites, and midwestern residents were more likely to visit a mental health specialist than their contemporaries in the South. In the multivariate analyses that follow, patients residing in midwestern states are the comparison group.

The impact of psychotherapy on multiple psychotropic prescribing was unclear, a priori. Patients who receive psychotherapy could be expected to be more likely to suffer from complicated conditions in which multiple psychotropic medications may be used. On the other hand, these patients may be more involved in treatment and less likely to use multiple drugs, depending on the training of the caregiver and the diagnosis.

METHOD

The NAMCS is conducted periodically by the National Center for Health Statistics (NCHS).²⁶ The 1989 survey included information regarding 38,384 patient visits representing estimates of 692 million visits to physicians throughout the United States. Seventy-four percent of the eligible physicians who were contacted (N = 1421) participated in the survey. Sample counties were stratified by size, region, and patient demographic characteristics, while the physicians sampled within counties were stratified by specialty and practice size.

For the purposes of this study, all visits of patients 18 years of age and older in which a psychotropic

Table 1. Total Psychotropic Medication Prescribing and Proportion Involving Multiple Psychotropics for Patients Older Than 18 Years of Age

Category	Total Visits Involving Drug	% All Office Visits	Visits With Single Drug in Category	Visits Involving Multiple Prescribing	% Visits Within Category With Multiple Prescribing
Antidepressant	12,081,940	1.74	8,568,899	3,513,041	29.1
Stimulant	395,810 ^a	.06	207,429	188,381 ^a	47.6
Antipsychotic	2,544,084	.37	1,187,937	1,356,147	53.3
Anorectic	1,003,759	.14	846,021	157,738 ^a	15.7
Anticholinergic	2,240,739	.32	1,676,834	563,905	25.2
Barbiturate	614,885	.09	598,924	15,961 ^a	2.6
Benzodiazepine	10,930,630	1.58	8,521,322	2,409,308	22.0
Anxiolytic	1,724,135	.25	1,487,087	237,048 ^a	13.7
Lithium	1,340,193	.19	383,123	957,070	71.4
Hypnotic	2,701,615	.39	1,768,610	933,005	34.5
Total	35,577,790	5.13	25,246,186	10,331,604	29.0

^aUnstable estimate, standard error > 30%.

medication was prescribed were abstracted for analysis. Medications were categorized according to the American Society of Hospital Pharmacists' drug classification scheme.²⁷ Two medications (both combining amitriptyline and perphenazine) were included in this study as combination products. ICD-9-CM (International Classification of Diseases, Ninth Revision, Clinical Modification) diagnoses were compiled into the same categories used by Hohmann et al.¹ Physician specialty was aggregated into three classes: general practice (general practice, family practice, and internal medicine), psychiatric specialty, and other (all other specialties).

The survey method used by NCHS requires the application of sampling weights to generate estimates of nationwide patient visits. In the descriptive tables that follow, weighted estimates of total visits and percentages are reported. The extrapolation of national visits from a limited sample creates potential problems with regard to the confidence level of estimates for rare occurrences. Estimates of national visits that have relative standard errors exceeding 30% are considered unreliable by the NCHS,²⁶ and are noted.

Multiple logistic regression methods were applied to the unweighted figures because parameter estimates and standard errors are not affected by sampling weights.²⁸ The categories of predictor variables were entered into the model sequentially, with the predisposing variables entered first, followed by enabling, need, and health services categories. This "step-up" procedure provides an estimate of the relative contribution of each domain to the probability that the attending physician ordered or provided multiple psychotropics during the patient visit. McFadden's pseudo- R^2 (similar to a log likelihood ratio) was used to compare the degree to which these categories improve predictive power.²⁸ Odds ratios and confidence intervals were calculated for significant explanatory variables using exponentiation.

RESULTS

Prevalence of Multiple Psychotropic Prescribing

Based on the NAMCS, the NCHS estimated that a total of 692.7 million patient visits occurred during 1989. As noted in Table 1, approximately 35.6 million patient visits involved at least one prescription for a psychotropic medication. These data show that certain categories of medications are more likely to involve multiple psychotropic prescribing. For example, lithium, antipsychotics, and stimulants are the most likely psychotropics to be used in combination with other psychotropics. It is important to note that medications in these three categories are infrequently prescribed, as the total use of all three constituted less than 1% of all office visits during 1989 (0.62%). The most frequent psychotropic medication combinations include antidepressants: benzodiazepines and antidepressants (24.5% of all combined psychotropics), antipsychotics and antidepressants (17.0%), and lithium and antidepressants (8.3%). Several other combinations are worthy of note, although the relatively small number of visits yields unreliable estimates: hypnotics and antidepressants (6.1%), antipsychotics and lithium (5.1%), and antipsychotics and anticholinergics (5.0%). An estimated 402,000 patient visits during 1989 involved the provision or ordering of two psychotropic medications within the same class.

Potentially Problematic Prescribing

Potentially problematic combinations could include duplicative therapy, offsetting therapy, or therapy in which there are no clinically accepted indications. Using this definition, nearly 2.8 million (27%) of the 10.3 million visits in which multiple psychotropic medications were prescribed occurred in combinations that could be considered therapeutically questionable.

Among the many combinations of psychotropic drugs represented in this sample, three appear with

Table 2. Logit Estimates of the Use of Multiple Psychotropic Medications*

Variable	β Estimate	β Estimate	β Estimate	β Estimate	Odds Ratio	Confidence Interval
Predisposing						
Age	-.014 ^a (16.29)	-.0006 (.01)	-.0001 (.0007)	-.000 (.000)		
Sex (1 = female)	-.019 (.02)	.104 (.54)	.068 (.22)	.071 (.24)		
Race (1 = minority)	-.185 (1.02)	-.25 (1.52)	-.322 (2.23)	-.305 (1.74)		
Enabling						
Other physician specialty		.022 (.01)	.147 (.55)	.173 (.75)	6.32	3.47, 11.51
Psychiatric specialty		2.06 ^a (167.72)	1.461 ^a (52.36)	1.844 ^a (36.37)		
HMO payment source		-.009 (.001)	.056 (.04)	-.026 (.009)		
Medicare payment source		-.012 (.003)	-.007 (.001)	.043 (.04)		
Medicaid payment source		.182 (.62)	.218 (.87)	.114 (.23)		
Need						
Psychiatric complaint			.308 (3.03)	.375 ^c (4.32)	1.45	1.02, 2.07
Neurologic diagnosis			.241 (1.57)	.322 (2.76)		
Stress diagnosis			.337 (.63)	.301 (.47)		
Depression diagnosis			.471 ^b (6.11)	.434 ^c (5.00)	1.54	1.06, 2.26
Schizophrenia diagnosis			.912 ^b (8.44)	1.10 ^a (11.72)	3.00	1.60, 5.62
Mania diagnosis			1.14 ^a (13.54)	1.42 ^a (19.60)	4.14	2.20, 7.71
Other psychoses diagnosis			.32 (1.12)	.367 (1.44)		
Other psychiatric diagnosis			.58 (1.74)	.77 (2.95)		
Repeat visit			.222 (.63)	.32 (1.29)		
Health services						
Psychotherapy provided				-.49 (2.83)		
Northeastern region				-.95 ^a (21.09)	.39	.26, .58
Southern region				-.46 ^a (7.10)	.63	.45, .89
Western region				-.33 (2.48)		
Model χ^2	17.56 ^a	260.19 ^a	285.36 ^a	311.85 ^a		
Pseudo-R ²	.0099	.147	.161	.176		

*Numbers in parentheses beside parameter estimates represent Wald chi-square estimates. The number of visits in the sample equals 2085.

^ap < .001, ^bp < .01, ^cp < .05.

sufficient frequency to merit concern: antidepressant and antipsychotic combinations; multiple concomitant central nervous system (CNS) depressants (including barbiturates, benzodiazepines, anxiolytics, and hypnotics); and CNS-stimulant/CNS-depressant combinations. Of the more than 12 million visits involving antidepressant drugs, almost 1.3 million (10.7%) also received an antipsychotic. Approximately 65% of this combination was prescribed by psychiatrists and virtually all of these were repeat visits for previously diagnosed problems. Psychotherapy services were provided during 64.0% of these visits.

A total of 639,580 visits involved multiple CNS depressants in 1989. Although this constituted less than 2% of all psychotropic visits, these combinations are notable. For example, while only about 4.3% of patients receiving a benzodiazepine also received a hypnotic drug, such a combination is rarely necessary. Less than 30% of this use occurred during visits to psychiatric specialists.

There was sufficient frequency of the combination of stimulant/anxiolytic, CNS depressant/stimulant, and anorectic/benzodiazepine to deserve mention, even though the low number of visits renders the estimates unreliable. It is notable that most of these combinations were prescribed by nonpsychiatrists, with the exception of the CNS depressant/stimulant category.

Fortunately, very few visits included CNS depressant/stimulant combinations (less than 94,000, or less than 0.3% of all visits involving psychotropics).

Nearly 54% of the potentially problematic combinations were prescribed by psychiatric specialties, while 32.0% were prescribed by general practice specialties. Approximately 58% of the questionable prescribing by psychiatrists was represented by the antidepressant/antipsychotic combination. Primary care physicians prescribed 47.0% of the combinations involving two or more medications within the same class (e.g., two antidepressants).

Factors Predicting Multiple Use

The multivariate analysis provides estimates of the factors that predict multiple psychotropic prescribing. The results in Table 2 show the strongest effects in the enabling, need, and health services categories. Variables within the predisposing category (age, sex, and race) did not predict the use of multiple psychotropic medications. The greatest increase in the pseudo-R² statistics occurred when the enabling characteristics were entered into the model.

Enabling. Psychiatric specialty was the only enabling variable to provide predictive power. As denoted by the odds ratios, this variable was the single strongest predictor of multiple psychotropic use. Spe-

cifically, patients who visit a psychiatrist were greater than six times more likely to receive an order for multiple psychotropic medications than patients who visit a general practice physician. Payment source did not prove to be a significant predictor of multiple use.

Need. Several variables in the need category demonstrated predictive power, although the category as a whole made only a modest contribution to the model's overall predictive power (an increase of less than 2% in the pseudo- R^2 statistic). The diagnostic classes were the best predictors in this category. Visits in which the physician identified a mania diagnosis were four times more likely to result in multiple psychotropic orders than visits in which a non-psychiatric diagnosis was specified. Visits with schizophrenia diagnoses were three times more likely than visits with only non-psychiatric diagnoses to result in the ordering of multiple psychotropic medications. Visits including depression diagnoses were approximately one and a half times more likely to result in such orders.

Health services. Regional differences provided the greatest predictive power in the health services category. As noted in Table 2, visits occurring in the northeastern and southern regions of the United States were much less likely to receive orders for multiple psychotropic medications than patients in the midwestern part of the country. Interestingly, visits in which psychotherapy was provided were not more likely to result in the prescribing of multiple psychotropics.

DISCUSSION

These results confirm previous studies that showed that psychiatric specialties are responsible for the majority of the multiple psychotropic prescribing.¹ Thus, it appears that primary care physicians and other non-psychiatrists either refer patients who present complicated psychiatric profiles to specialists, may not recognize the more complex diagnostic issues, or simply do not use multiple psychotropics to treat such patients. The small proportion of multiple psychotropic medication visits to nonpsychiatrists provides preliminary evidence that these physicians may recognize the difficulties associated with treating more complicated psychiatric cases.

The relatively low incidence of multiple psychotropic prescribing within individual categories should be cause for some celebration, but there is cause for concern, as well. Nearly 40% of all multiple psychotropic prescribing reported in the NAMCS data occurred in categories with no readily apparent clinical justification. The results addressing the three potentially problematic categories (antidepressant and antipsychotic; multiple concomitant CNS depressants; and

CNS depressant and stimulant combinations) deserve particular mention. These combinations are particularly worrisome because of the lack of clinical support for their frequent use.

While there are several indications for the combination of an antipsychotic drug with an antidepressant, these indications are infrequent. Schizophrenic patients, who require chronic antipsychotic drug therapy, may at times experience major depressive episodes necessitating drug treatment.²⁹ Also, patients with a major depressive disorder may infrequently experience psychotic symptoms.³⁰ Psychotic depression must often be treated acutely with both an antidepressant drug and an antipsychotic drug, but there is no evidence to support a role for antipsychotic drug therapy in nonpsychotic depression.³¹ It is impossible in this study to determine whether the nearly 11% of patients receiving an antidepressant and antipsychotic drug meet one of these two conditions. However, the combination of antidepressant and antipsychotic is often used for either anxious nonpsychotic depression or for an inadequately diagnosed patient where drug therapy is being used as a diagnostic tool. Both situations are problematic. Use of an antipsychotic drug for anxiety or agitation that accompanies depression is rarely appropriate when safer and more effective antianxiety drugs can be used. Use of an antipsychotic drug, merely for its sedative effect and the risk of tardive dyskinesia, in a patient without psychotic symptoms is of even greater concern than the lack of any documented evidence of benefit. Diagnostic uncertainty also accounts for some of the use of combination psychotropic drugs. However, success or failure of combination therapy does not help clarify the diagnosis as would use of a single drug trial.

The primary concern regarding the combination of CNS depressants is unnecessary drug duplication. At best, the use of multiple CNS depressants represents unnecessary use of additional drugs. Selection of an antianxiety drug should include consideration of desired onset of effect, elimination half-life, and a dose and dosage schedule that matches the symptoms and needs of the patient. It is rarely necessary to prescribe one antianxiety drug for the daytime and another drug for sleep at night. It is also rarely necessary to use two benzodiazepines or two anxiolytic drugs together except during a transition from one to another.³² For some patients, however, multiple CNS depressants pose the risk of serious adverse effects such as excessive sedation, impaired psychomotor performance, ataxia, and possible falls.^{33,34}

The multivariate results provide strong evidence that multiple psychotropic use is related to psychiatric specialty. This fact, combined with the descriptive data showing that patients in the antidepressant/anti-

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