

# National Patterns in Antidepressant Medication Treatment

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**Context:** Antidepressants have recently become the most commonly prescribed class of medications in the United States.

**Objective:** To compare sociodemographic and clinical patterns of antidepressant medication treatment in the United States between 1996 and 2005.

**Design:** Analysis of antidepressant use data from the 1996 (n=18 993) and 2005 (n=28 445) Medical Expenditure Panel Surveys.

**Setting:** Households in the United States.

**Participants:** Respondents aged 6 years or older who reported receiving at least 1 antidepressant prescription during that calendar year.

**Main Outcome Measures:** Rate of antidepressant use and adjusted rate ratios (ARRs) of year effect on rate of antidepressant use adjusted for age, sex, race/ethnicity, annual family income, self-perceived mental health, and insurance status.

**Results:** The rate of antidepressant treatment increased from 5.84% (95% confidence interval [CI], 5.47-6.23) in 1996 to 10.12% (9.58-10.69) in 2005 (ARR, 1.68;

95% CI, 1.55-1.81), or from 13.3 to 27.0 million persons. Significant increases in antidepressant use were evident across all sociodemographic groups examined, except African Americans (ARR, 1.13; 95% CI, 0.89-1.44), who had comparatively low rates of use in both years (1996, 3.61%; 2005, 4.51%). Although antidepressant treatment increased for Hispanics (ARR, 1.75; 95% CI, 1.60-1.90), it remained comparatively low (1996, 3.72%; 2005, 5.21%). Among antidepressant users, the percentage of patients treated for depression did not significantly change (1996, 26.25% vs 2005, 26.85%; ARR, 0.95; 95% CI, 0.83-1.07), although the percentage of patients receiving antipsychotic medications (5.46% vs 8.86%; ARR, 1.77; 95% CI, 1.31-2.38) increased and those undergoing psychotherapy declined (31.50% vs 19.87%; ARR, 0.65; 95% CI, 0.56-0.72).

**Conclusions:** From 1996 to 2005, there was a marked and broad expansion in antidepressant treatment in the United States, with persisting low rates of treatment among racial/ethnic minorities. During this period, individuals treated with antidepressants became more likely to also receive treatment with antipsychotic medications and less likely to undergo psychotherapy.

*Arch Gen Psychiatry.* 2009;66(8):848-856

**I**N THE UNITED STATES, THERE HAS been a recent increase in the percentage of persons receiving mental health treatment each year. Among nonelderly adults, the percentage increased from 12.2% in 1990-1992 to 20.1% in 2001-2003.<sup>1</sup> Several factors may have contributed to this trend, including a broadening in concepts of need for mental health treatment,<sup>2</sup> campaigns to promote mental health care,<sup>3</sup> and growing public acceptance of mental health treatments.<sup>4</sup>

In parallel with growth in mental health service usage, psychotropic medications have become increasingly prominent in treatment. The percentage of the US population using at least 1 psychotropic medication increased from 5.9% in 1996 to 8.1% in 2001.<sup>5</sup> Among the psychotropic drugs, antidepressants are the most frequently

prescribed medications.<sup>6,7</sup> In 2005, antidepressants surpassed antihypertensive agents to become the most commonly prescribed class of medications in office-based<sup>6</sup> and hospital outpatient-based<sup>7</sup> medical practice.

Antidepressant use by adults and youths has increased in the United States. According to the National Health and Nutrition Examination Surveys, the monthly rate of antidepressant use among adults increased from 2.5% in 1988-1994 to 8.1% in 1999-2001.<sup>8</sup> Data from the National Comorbidity Surveys indicate that among adults aged 15 to 54 years, use of an antidepressant in the last year because of mental health reasons increased from 2.2% in 1990-1992 to 10.1% in 2001-2003.<sup>9</sup> Medical Expenditure Panel Survey (MEPS) data reveal that annual antidepressant use among youths younger than 19 years increased

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from 1.3% in 1997 to 1.8% in 2002.<sup>10</sup> National ambulatory care surveys<sup>11</sup> and administrative data from a large health maintenance organization<sup>12</sup> also demonstrate increased use of antidepressants by young persons. These earlier reports have not provided information about concomitant psychotropic medication use, psychotherapy, or the conditions for which antidepressants are prescribed. Such information would provide a clinical context in which to assess recent national trends in antidepressant use.

The present study examined trends in antidepressant use between 1996 and 2005 in a nationally representative sample of household members aged 6 years and older. Secular trends are presented in the rate of antidepressant use stratified by sociodemographic and clinical characteristics. In antidepressant users, changes are described in their sociodemographic and clinical characteristics and in the mean annual number of filled prescriptions for antidepressants.

## METHODS

### SOURCES OF DATA

Data were drawn from the household component of the 1996 and 2005 Medical Expenditure Panel Surveys (MEPSs).<sup>13,14</sup> Both surveys were sponsored by the Agency for Healthcare Research and Quality to provide national estimates of the use, expenditures, and financing of health services. The MEPSs are conducted as national probability samples of the US civilian noninstitutionalized population and are designed to provide nationally representative estimates for comparisons over time.

The 1996 MEPS household component was drawn from a nationally representative subsample of the 1995 National Health Interview Survey. A sample of 21 571 participants provided data for the entire 1996 survey year. This represents a full-year response rate of 70.2% after factoring in the effects of nonresponse to the National Health Interview Survey and to the first round of MEPS, and survey attrition. A sample of 32 320 participants provided data for the entire 2005 survey for a full-year response rate of 61.3% (household component for 2005). For both surveys, a designated adult informant was queried about all related persons who lived in the household. The analysis is limited to participants aged 6 years or older during the 1996 (n = 18 993) and 2005 (n = 28 445) surveys.

The Agency for Healthcare Research and Quality devised weights and design variables to adjust for the complex survey sample and yield unbiased national estimates. The sampling weights also adjust for nonresponse and poststratification to population totals based on US census data as described elsewhere.<sup>15</sup>

### STRUCTURE OF SURVEY

Households selected for the 1996 and 2005 MEPS household surveys were interviewed in person 3 times to obtain health care utilization information for the survey calendar year. In both surveys, respondents were asked to record medical events as they occurred in a calendar or diary that was reviewed during each interview. Written permission was obtained from survey participants to contact medical providers whom they or household members reported seeing during the survey period. Survey staff contacted medical providers to supplement and validate diagnostic and other clinical information about the medical visits reported by the respondents. The medical provider data validation included all hospitals, hospital physicians, home health agencies, and pharmacies reported by survey respondents.

## TREATMENT WITH ANTIDEPRESSANT AND OTHER PSYCHOTROPIC MEDICATIONS

The MEPS ask for all prescribed medicines associated with each health care visit. Respondents are asked to supply the names of any prescribed medications purchased or otherwise obtained, the first and last dates taken, the number of times obtained, and the conditions associated with each medicine, and then they are asked for permission to collect more detailed information from their local pharmacies. At the pharmacies, data are collected about the type, dosage, and payment for each filled prescription. Psychotropic medications were classified as antidepressant, anxiolytic, or antipsychotic agents; mood stabilizers; or stimulants. Antidepressants were subclassified as selective serotonin reuptake inhibitors (fluoxetine hydrochloride, sertraline hydrochloride, paroxetine hydrochloride, fluvoxamine maleate, citalopram hydrobromide, and escitalopram oxalate), other newer antidepressants (venlafaxine hydrochloride, duloxetine hydrochloride, mirtazapine, and bupropion hydrochloride), and tricyclic antidepressants and other older antidepressants. Anxiolytics included benzodiazepines, zolpidem tartrate, zaleplon, buspirone hydrochloride, short-acting barbiturates, meprobamate, and chloral hydrate. Antipsychotics included both older agents and newer atypical antipsychotic medications but excluded antipsychotics largely limited to the control of allergic rhinitis (promethazine hydrochloride) or nausea and vomiting (droperidol, prochlorperazine maleate, and promethazine hydrochloride). Mood stabilizers included lithium carbonate, lithium citrate, carbamazepine, divalproex sodium/valproic acid/valproate sodium, and lamotrigine in the absence of treatment for a seizure disorder (*International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM]* code 345). A post hoc analysis included these medications as well as treatments with unproved efficacy including gabapentin, oxcarbazepine, and topiramate.<sup>16</sup>

### TREATED CONDITIONS

Respondents were asked the reason for every outpatient visit during the reference period. Conditions were recorded by interviewers as verbatim text and then subsequently coded by professional coders according to the ICD-9-CM as revised for the National Health Interview Survey. Interviewers each underwent 80 hours of training, and coders all had degrees in nursing or medical record administration. A total of 5% of records were rechecked for errors; error rates in these rechecks were less than 2.5%. A staff psychiatric nurse established mental disorder diagnoses when there was diagnostic ambiguity or uncertainty. Respondents who made 1 outpatient visit or more coded for the purpose of treating ICD-9-CM and *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition) codes 296.2, 296.3, 298.0, 300.4, 309.1, or 311 were defined as having received treatment for a depressive disorder. Similar criteria were applied to define treatment for anxiety disorder (codes 293.84, 300.0, 300.2, 300.3, 308.3, and 309.8), bipolar disorder (codes 296.0, 296.4-296.8, and 301.13), and adjustment-related disorders (codes 309.0, 309.1, 309.2, 309.4, 309.9, and 308).

Using the methods of Blanco et al.,<sup>17</sup> respondents were defined as receiving treatment for ICD-9-CM conditions for which the effectiveness of antidepressants has been studied<sup>18</sup> including headache (codes 784.0, 346.1, 346.2, and 307.81), back pain (codes 721.2-721.9, 722.1, 722.2, 722.3, 722.5-722.9, and 724), neuropathy (codes 351-357), sleep-related conditions (codes 780.5, 307.4, 327.8, 327.0, and 327.1), and fatigue (codes 780.7). Respondents rated their mental health as excellent, very good, good, fair, or poor at the first of the 3 in-person interviews.

## MENTAL HEALTH CARE

The MEPS booklets solicit information on the type of health care professionals providing treatment at each visit. We classified mental health care professionals as social workers (1996 and 2005), psychologists (1996 and 2005), and psychiatrists (2005).

The MEPS asked respondents the type of care provided during each outpatient visit using a card with various response categories. A dichotomous variable defined each respondent based on the presence of 1 visit or more that included a specific indication of "psychotherapy/mental health counseling." Separate variables classified emergency department visits and inpatient admissions during each survey with a primary diagnosis of a mental disorder (*ICD-9-CM* codes 290-319). Medical providers were contacted by telephone to obtain information such as visit date or diagnosis that household respondents were unable to confirm.<sup>13</sup>

### ANALYSIS PLAN

Rates of antidepressant treatment per 100 persons were determined overall in each survey year and stratified by respondent sex, age group, race/ethnicity, marital status, educational achievement, health insurance group, employment status, and selected treatment condition group. Overall and within each stratum, a series of log-linear models were fit to evaluate the effect of survey year on the relative rate ratio of treatment with an antidepressant, controlling for respondent age, sex, race/ethnicity, annual family income, health insurance group, and mental health status (excellent, very good, or good vs fair or poor). Total annual family income was considered as low (<200% of poverty threshold), medium (200% to <400% of poverty threshold), or high ( $\geq 400\%$  of poverty threshold).

An examination was also made of the clinical characteristics of individuals who reported receiving treatment with antidepressants in each survey year. Patients treated with antidepressants in 1996 and 2005 were compared for antidepressant type, treatment with other classes of psychotropic medications, treatment by mental health professional groups, mental health service use, and selected treated conditions. Among respondents treated with antidepressants, a series of log-linear regression models were fit, controlling for respondent age, sex, race/ethnicity, annual family income, mental health status, and insurance group to estimate the effect of survey year on the distribution of selected respondent characteristics. Results are presented as adjusted rate ratios (ARRs) with 95% confidence intervals (CIs). When CIs of ARRs of antidepressants did not overlap between strata, a  $z$  test was used to assess whether the ARRs differed across strata ( $\alpha < .05$ ). Analogous analyses were also performed to examine trends in the annual number of antidepressant prescriptions filled overall and stratified by sociodemographic groups. A similar analysis was conducted of the subgroup of antidepressant users who underwent psychotherapy in a given year. All statistical analyses were performed using commercially available software (SUDAAN; RTI International, Research Triangle Park, North Carolina) to accommodate the complex sample design and the weighting of observations.

## RESULTS

### RATES OF ANTIDEPRESSANT TREATMENT

Between 1996 and 2005, the overall annual rate of antidepressant treatment among persons 6 years and older

increased from 5.84 to 10.12 per 100 persons (**Table 1**). This corresponds to a national increase from 13.3 million persons in 1996 to 27.0 million persons in 2005 treated with antidepressants.

A significant increase in the rate of antidepressant treatment was observed for male and female individuals of all ages, marital status, educational achievement, and health insurance groups and for employed and unemployed adults (Table 1). The rate of antidepressant treatment did not significantly increase among African Americans. In a post hoc analysis, the ARR for white respondents significantly differed from that for African American respondents ( $z=3.32$ ;  $P < .001$ ) (data not shown). Among African American and Hispanic respondents, the rate of antidepressant treatment remained well below the rate for white respondents (Table 1).

In the multivariate models of selected treated conditions, treatment of anxiety, depression, and adjustment disorders were associated with a significant increase in antidepressant treatment. The increase in antidepressant treatment of bipolar disorder, although substantial, was not statistically significant. Treatment of back pain and neuropathy but not headache, fatigue, or sleep-related disorders was also associated with increased antidepressant treatment (**Table 2**). Increases in antidepressant treatment were especially evident in persons with excellent, very good, or good self-rated mental health (Table 2). A post hoc analysis revealed that the ARR for respondents with excellent, very good, or good self-rated mental health was significantly greater than that for respondents with poor or fair self-rated mental health ( $z=4.65$ ;  $P < .001$ ) (data not shown).

### CHARACTERISTICS OF PERSONS TREATED WITH ANTIDEPRESSANTS

Among persons treated with antidepressants, use of selective serotonin reuptake inhibitors and other newer antidepressants became increasingly common and use of tricyclic antidepressants became less common (**Table 3**). There was also a significant increase in the percentage of antidepressant users treated with antipsychotic medications, although there was a decrease in the percentage who received inpatient treatment for a mental disorder or psychotherapy (Table 3). Among persons prescribed antidepressants in 2005, 34.59% (95% CI, 30.39-39.05) of those treated by psychiatrists and 7.46% (95% CI, 6.28-8.85) of those treated by nonpsychiatrist physicians also received either mood stabilizers or antipsychotic medications. If medications that are sometimes used clinically as mood stabilizers but are of unproved efficacy (gabapentin, oxcarbazepine, and topiramate) are added, these percentages increase to 39.83% (95% CI, 35.53-44.29) for psychiatrists and 13.12% (95% CI, 11.47-14.97) for nonpsychiatrist physicians (data not shown).

Among persons treated with antidepressants who underwent psychotherapy, the mean (SE) number of psychotherapy visits per subject during the survey year remained little changed from 9.89 (0.86) in 1996 to 10.17 (0.94) in 2005 ( $t=-0.22$ ;  $P=.83$ ) (data not shown). A minority of antidepressant users were treated for any mental disorder (1996, 42.05%; 95% CI, 38.73-45.45; and

**Table 1. Rates per 100 Persons Treated With Antidepressants in the United States, 1996 and 2005, Total and Stratified by Sociodemographic Characteristics**

Characteristic	Yearly Rate per 100 Persons, % (95% CI)		
	MEPS 1996	MEPS 2005	ARR <sup>a</sup>
Total (n <sub>1</sub> = 18 993; n <sub>2</sub> = 28 445)	5.84 (5.47-6.23)	10.12 (9.58-10.69)	1.68 (1.55-1.81)
Sex			
Male (n <sub>1</sub> = 9003; n <sub>2</sub> = 13 404)	3.96 (3.56-4.41)	6.68 (6.10-7.30)	1.68 (1.47-1.92)
Female (n <sub>1</sub> = 9990; n <sub>2</sub> = 15 041)	7.62 (7.03-8.25)	13.42 (12.67-14.22)	1.69 (1.54-1.85)
Age, y			
6-17 (n <sub>1</sub> = 4182; n <sub>2</sub> = 6465)	1.44 (1.08-1.90)	2.56 (2.02-3.24)	1.68 (1.19-2.37)
18-34 (n <sub>1</sub> = 4926; n <sub>2</sub> = 7041)	4.15 (3.52-4.89)	6.82 (6.02-7.71)	1.67 (1.38-2.02)
35-49 (n <sub>1</sub> = 4743; n <sub>2</sub> = 6564)	7.40 (6.57-8.33)	13.21 (12.12-14.38)	1.78 (1.54-2.04)
50-64 (n <sub>1</sub> = 2793; n <sub>2</sub> = 4901)	8.68 (7.57-9.93)	15.55 (14.40-16.77)	1.74 (1.49-2.03)
≥65 (n <sub>1</sub> = 2349; n <sub>2</sub> = 3474)	9.80 (8.53-11.24)	13.69 (12.31-15.19)	1.46 (1.23-1.73)
Race/ethnicity			
White <sup>b</sup> (n <sub>1</sub> = 12 645; n <sub>2</sub> = 16 315)	6.48 (6.04-6.94)	11.96 (11.27-12.68)	1.46 (1.13-1.88)
Black (n <sub>1</sub> = 2501; n <sub>2</sub> = 4621)	3.61 (2.99-4.34)	4.51 (3.84-5.29)	1.13 (.89-1.44)
Hispanic (n <sub>1</sub> = 3847; n <sub>2</sub> = 7509)	3.72 (2.93-4.71)	5.21 (4.52-5.99)	1.75 (1.60-1.90)
Marital status <sup>c</sup>			
Married (n <sub>1</sub> = 8656; n <sub>2</sub> = 11 881)	6.63 (6.05-7.26)	11.93 (11.16-12.74)	1.77 (1.59-1.97)
Not married (n <sub>1</sub> = 2494; n <sub>2</sub> = 4192)	5.17 (4.21-7.75)	8.63 (7.64-9.74)	1.58 (1.25-2.00)
Separated/divorced (n <sub>1</sub> = 1771; n <sub>2</sub> = 2988)	10.18 (8.45-12.20)	16.41 (14.71-18.26)	1.56 (1.28-1.90)
Widowed (n <sub>1</sub> = 1087; n <sub>2</sub> = 1591)	11.25 (9.38-13.43)	17.41 (15.29-19.76)	1.58 (1.27-1.96)
Educational achievement, highest grade <sup>c</sup>			
0-11 (n <sub>1</sub> = 3446; n <sub>2</sub> = 5243)	8.42 (7.49-9.46)	11.40 (10.21-12.72)	1.50 (1.29-1.74)
12-15 (n <sub>1</sub> = 7483; n <sub>2</sub> = 10 807)	6.93 (6.29-7.63)	12.82 (12.04-13.70)	1.73 (1.55-1.94)
>16 (n <sub>1</sub> = 2953; n <sub>2</sub> = 4434)	6.54 (5.54-7.70)	11.85 (10.84-12.98)	1.71 (1.42-2.05)
Family income <sup>c</sup>			
Low (n <sub>1</sub> = 7220; n <sub>2</sub> = 12 189)	6.46 (5.79-9.61)	10.40 (9.61-11.25)	1.57 (1.39-1.77)
Medium (n <sub>1</sub> = 5877; n <sub>2</sub> = 8070)	5.28 (4.71-5.90)	9.94 (9.06-10.88)	1.80 (1.59-2.06)
High (n <sub>1</sub> = 5896; n <sub>2</sub> = 8186)	5.77 (5.19-6.40)	10.07 (9.31-10.86)	1.68 (1.48-1.91)
Health insurance			
Private (n <sub>1</sub> = 13 185; n <sub>2</sub> = 16 686)	5.75 (5.32-6.22)	10.28 (9.64-10.95)	1.75 (1.59-1.92)
Public (n <sub>1</sub> = 3039; n <sub>2</sub> = 6928)	9.05 (7.90-10.35)	13.68 (12.55-14.89)	1.56 (1.34-1.81)
None (n <sub>1</sub> = 2769; n <sub>2</sub> = 4831)	2.95 (2.31-3.78)	4.75 (4.06-5.56)	1.44 (1.08-1.92)
Employment status <sup>d</sup>			
Employed (n <sub>1</sub> = 9451; n <sub>2</sub> = 13 297)	5.23 (4.75-5.76)	9.80 (9.10-10.54)	1.83 (1.62-2.06)
Unemployed (n <sub>1</sub> = 2209; n <sub>2</sub> = 3809)	13.05 (11.39-14.91)	21.59 (19.74-23.55)	1.61 (1.38-1.87)

Abbreviations: ARR, adjusted rate ratio; CI, confidence interval; MEPS, Medical Expenditure Panel Survey; n<sub>1</sub>, MEPS 1996; n<sub>2</sub>, MEPS 2005.

<sup>a</sup>Adjusted for age, sex, race/ethnicity, annual family income, mental health status, and health insurance.

<sup>b</sup>Includes white, American Indian, Alaska Native, and Asian or Pacific Islander.

<sup>c</sup>See "Analysis Plan" subsection of the "Methods" section for an explanation of the classification of total annual family income.

<sup>d</sup>Limited to respondents aged 21 years or older.

2005, 42.30%; 95% CI, 39.97-44.65). There was a significant increase in the ARR for antidepressant users treated for bipolar, anxiety, or sleep-related disorders and a significant decrease in the ARR for those treated for headache (Table 3).

#### ANNUAL ANTIDEPRESSANT PRESCRIPTIONS

There was an overall increase in the mean number of antidepressant prescriptions, from 5.60 in 1996 to 6.93 in 2005 among treated individuals (Table 4). In stratified analyses, significant increases in the mean number of antidepressant prescriptions were observed in all sociodemographic groups except youths (age 6-17 years), young adults (age 18-34 years), older adults (age >65 years), Hispanics, and uninsured persons. Significant increases in the mean number of antidepressant prescriptions also were noted for persons treated with selective serotonin reuptake inhibitors (adjusted  $\beta=1.11$ ;  $P=.001$ ), other

newer antidepressants (adjusted  $\beta=1.83$ ;  $P<.001$ ), and tricyclic antidepressants (adjusted  $\beta=1.64$ ;  $P<.001$ ) (data not shown).

#### COMMENT

Between 1996 and 2005 in the United States, the percentage of persons aged 6 years and older treated with an antidepressant medication during the course of 1 year increased from 5.8% to 10.1%, or from approximately 13.3 to 27.0 million persons. These findings update earlier reports of increasing antidepressant use<sup>8-12</sup> and provide new information about the changing clinical characteristics of US residents treated with antidepressants. Significant increases in antidepressant use were evident for all major sociodemographic groups except African Americans, who had relatively low rates of antidepressant use in both national surveys. Among antidepressant users,

**Table 2. Rates per 100 Persons Treated With Antidepressants in the United States, 1996 and 2005, Stratified by Clinical Characteristics<sup>a</sup>**

Characteristic	Yearly Rate per 100 Persons, % (95% CI)		
	MEPS 1996	MEPS 2005	ARR <sup>a</sup>
Total (n <sub>1</sub> = 18 993; n <sub>2</sub> = 28 445)	5.84 (5.47-6.23)	10.12 (9.58-10.69)	1.68 (1.55-1.81)
Mental health status <sup>b</sup>			
Excellent to good (n <sub>1</sub> = 17 837; n <sub>2</sub> = 26 392)	4.58 (4.22-4.96)	8.47 (8.00-8.96)	1.84 (1.67-2.02)
Fair to poor (n <sub>1</sub> = 1147; n <sub>2</sub> = 1983)	27.11 (24.03-30.42)	35.32 (32.42-38.34)	1.21 (1.05-1.39)
Selected treated condition group <sup>c</sup>			
Depression (n <sub>1</sub> = 425; n <sub>2</sub> = 951)	72.11 (67.40-76.37)	80.32 (76.68-83.52)	1.10 (1.03-1.19)
Bipolar disorder (n <sub>1</sub> = 35; n <sub>2</sub> = 149)	52.23 (37.25-66.83)	65.35 (55.67-73.90)	1.29 (0.94-1.76)
Anxiety (n <sub>1</sub> = 177; n <sub>2</sub> = 579)	49.27 (42.04-56.53)	66.03 (61.18-70.57)	1.34 (1.14-1.58)
Adjustment (n <sub>1</sub> = 112; n <sub>2</sub> = 215)	22.26 (14.89-31.90)	39.37 (31.53-47.79)	1.92 (1.26-2.95)
Headache (n <sub>1</sub> = 359; n <sub>2</sub> = 522)	27.22 (22.17-32.94)	29.67 (25.92-34.59)	1.10 (0.87-1.41)
Back pain (n <sub>1</sub> = 967; n <sub>2</sub> = 1672)	14.15 (11.91-16.72)	22.90 (20.65-25.32)	1.54 (1.27-1.87)
Neuropathy (n <sub>1</sub> = 212; n <sub>2</sub> = 340)	18.56 (13.36-25.20)	30.99 (26.05-36.40)	1.44 (1.02-2.03)
Fatigue (n <sub>1</sub> = 73; n <sub>2</sub> = 97)	32.58 (22.52-44.53)	33.45 (23.08-45.07)	0.95 (0.60-1.49)
Sleep disorder (n <sub>1</sub> = 84; n <sub>2</sub> = 323)	45.35 (35.38-55.71)	45.46 (38.99-52.09)	1.01 (0.79-1.29)

Abbreviations: ARR, adjusted rate ratio; CI, confidence interval; MEPS, Medical Expenditure Panel Survey; n<sub>1</sub>, MEPS 1996; n<sub>2</sub>, MEPS 2005.

<sup>a</sup>Adjusted for age, sex, race/ethnicity, annual family income, mental health status, and health insurance.

<sup>b</sup>Because of missing data, the subpopulations do not sum to the totals.

<sup>c</sup>See the "Treated Conditions" subsection of the "Methods" section for more detailed descriptions of the treated conditions.

**Table 3. Clinical Characteristics of Persons Treated With Antidepressants in the United States, 1996 and 2005**

Characteristics	Percentage (95% CI)		
	MEPS 1996 (n = 1029)	MEPS 2005 (n = 2602)	ARR <sup>a</sup>
Antidepressant use			
SSRIs	54.80 (51.47-58.09)	66.89 (64.70-69.02)	1.22 (1.14-1.30)
Other new agents	23.64 (21.08-26.41)	37.87 (35.57-40.21)	1.60 (1.41-1.82)
TCA	35.32 (32.10-38.69)	11.09 (9.71-12.64)	0.32 (0.27-.37)
Other psychotropic drugs			
Any	36.71 (33.59-39.94)	38.13 (35.98-40.33)	0.99 (0.89-1.11)
Anxiolytics/hypnotics	23.97 (21.26-26.90)	24.31 (22.29-26.45)	1.03 (0.89-1.19)
Antipsychotics	5.46 (4.19-7.09)	8.86 (7.69-10.19)	1.77 (1.31-2.38)
Mood stabilizers	8.21 (6.61-10.17)	5.91 (4.85-7.18)	0.79 (0.59-1.05)
Stimulants	3.97 (2.71-5.79)	5.70 (4.95-6.84)	1.38 (0.94-2.01)
Mental health professional			
Psychiatrist	...	19.05 (17.02-21.25)	...
Psychologist	10.64 (8.80-12.82)	8.68 (7.47-10.47)	0.82 (0.64-1.05)
Social worker	4.63 (3.35-6.37)	4.19 (3.21-5.21)	0.97 (0.64-1.47)
Mental health service			
Psychotherapy	31.50 (28.15-35.05)	19.87 (18.01-21.87)	0.65 (0.56-0.72)
Emergency department	1.76 (1.09-2.82)	1.65 (1.18-2.32)	0.97 (0.55-1.72)
Inpatient	3.93 (2.87-5.37)	2.08 (1.53-2.82)	0.60 (0.39-0.92)
Selected treated conditions			
Depression	26.25 (26.30-32.39)	26.85 (24.98-28.81)	0.95 (0.83-1.07)
Bipolar disorder	1.81 (1.09-3.01)	3.25 (2.49-4.23)	2.05 (1.14-3.67)
Anxiety	8.55 (6.92-10.52)	14.14 (12.70-15.71)	1.70 (1.34-2.15)
Adjustment	2.20 (1.46-3.29)	3.34 (2.58-4.30)	1.49 (0.91-2.42)
Headache	8.82 (7.04-11.01)	5.46 (4.52-6.58)	0.63 (0.47-.84)
Back pain	12.95 (10.83-15.41)	15.17 (13.68-16.80)	1.16 (0.95-1.43)
Neuropathy	3.77 (2.87-5.37)	3.99 (3.25-4.88)	0.97 (0.65-1.45)
Fatigue	2.47 (1.60-3.81)	1.39 (0.93-2.08)	0.55 (0.30-1.00)
Sleep disorder	3.77 (2.87-5.37)	5.34 (4.43-6.43)	1.42 (1.02-1.98)
Mental health status			
Excellent to good	74.84 (71.13-78.23)	78.97 (76.97-80.85)	1 [Reference]
Fair to poor	25.16 (21.77-28.87)	19.15 (23.04-14.13)	0.97 (0.94-1.00)

Abbreviations: ARR, adjusted rate ratio; CI, confidence interval; ellipses, data not available; MEPS, Medical Expenditure Panel Survey; SSRIs, selective serotonin reuptake inhibitors; TCA, tricyclic antidepressants.

<sup>a</sup>Adjustment for age, sex, race/ethnicity, annual income, mental health status, and health insurance.

**Table 4. Number of Antidepressant Prescriptions in Persons Treated With Antidepressants in the United States, 1996 and 2005, Total and Stratified by Sociodemographic Groups<sup>a</sup>**

Group Characteristic	No. of Antidepressant Prescriptions		Statistics		Adjusted Year Effect <sup>b</sup>	
	MEPS 1996 (n = 1029)	MEPS 2005 (n = 2602)	t	P Value	β	P Value
	Mean (SE)	Mean (SE)				
Total	5.60 (0.17)	6.93 (0.15)	5.93	<.001	1.41	<.001
Sex						
Male	5.27 (0.24)	6.61 (0.21)	4.13	<.001	1.49	<.001
Female	5.76 (0.21)	7.09 (0.17)	4.89	<.001	1.30	<.001
Age, y						
6-17	4.95 (0.75)	6.51 (0.56)	1.66	.10	1.11	.23
18-34	5.09 (0.34)	5.34 (0.26)	0.57	.57	0.54	.20
35-49	5.75 (0.28)	7.57 (0.28)	4.59	<.001	1.97	<.001
50-64	5.53 (0.29)	7.44 (0.24)	5.11	<.001	1.95	<.001
≥65	6.04 (0.37)	6.63 (0.31)	1.21	.23	0.73	.13
Race/ethnicity						
White <sup>c</sup>	5.73 (0.19)	7.08 (0.16)	5.46	<.001	1.39	<.001
Black	4.88 (0.47)	6.48 (0.42)	2.53	.01	1.43	.02
Hispanic	4.69 (0.44)	5.45 (0.39)	1.28	.20	0.81	.16
Marital status <sup>d</sup>						
Married	5.55 (0.25)	6.67 (0.17)	3.71	<.001	1.15	<.001
Not married	5.71 (0.43)	6.92 (0.47)	1.91	.06	1.27	.04
Separated/divorced	5.84 (0.35)	7.96 (0.36)	4.22	<.001	2.04	<.001
Widowed	5.72 (0.37)	7.08 (0.44)	2.37	.02	1.49	.01
Educational achievement level, highest grade <sup>d</sup>						
0-11	5.68 (0.32)	7.68 (0.33)	4.34	<.001	2.17	<.001
12-15	5.70 (0.28)	7.02 (0.18)	3.96	<.001	1.18	<.001
≥16	5.54 (0.34)	6.52 (0.29)	2.23	.03	1.23	.01
Family income <sup>d</sup>						
Low	5.92 (0.30)	7.50 (0.26)	4.00	<.001	1.61	<.001
Medium	4.97 (0.25)	6.74 (0.24)	5.15	<.001	1.66	<.001
High	5.78 (0.37)	6.64 (0.18)	2.11	.04	0.89	.03
Health insurance						
Private	5.51 (0.20)	6.77 (0.16)	4.86	<.001	1.31	<.001
Public	6.07 (0.38)	7.83 (0.29)	3.67	<.001	1.79	<.001
None	5.14 (0.54)	5.61 (0.38)	0.71	.48	0.88	.16
Employment status <sup>e</sup>						
Employed	5.13 (0.23)	6.48 (0.18)	4.72	<.001	1.37	<.001
Unemployed	6.28 (0.34)	8.26 (0.29)	4.42	<.001	2.05	<.001

Abbreviation: MEPS, Medical Expenditure Panel Survey.

<sup>a</sup>Mean represents mean number of antidepressant prescriptions in strata during survey year.

<sup>b</sup>Adjusted for age, sex, race/ethnicity, annual family income, mental health status, and health insurance.

<sup>c</sup>Includes white, American Indian, Alaska native, and Asian or Pacific Islander.

<sup>d</sup>See "Analysis Plan" subsection of the "Methods" section for an explanation of the classification of total annual family income.

<sup>e</sup>Limited to respondents aged 21 years and older.

the percentage who also received antipsychotic medications increased, whereas the percentage who also underwent psychotherapy declined. Together with an increase in the number of antidepressant prescriptions per antidepressant user, these broad trends suggest that antidepressant treatment is occurring within a clinical context that places greater emphasis on pharmacologic rather than psychologic dimensions of care.

Several factors may have contributed to the increased use of antidepressant medications. Perhaps most important, major depression may have become more common. Two large cross-sectional nationally representative surveys indicate that the prevalence of major depression in adults increased from 3.3% in 1991-1992 to 7.1% in 2001-2002.<sup>19</sup> In addition, several antidepressants including mirtazapine (1996), citalo-

pram (1998), fluvoxamine (2000), and escitalopram (2002) were approved by the US Food and Drug Administration to treat depressive and anxiety disorders during the study period. Several clinical guidelines were also published supporting the use of antidepressants for a variety of conditions including anxiety disorders<sup>20,21</sup> and other conditions.<sup>22-24</sup> Although there was little change in total promotional spending for antidepressants between 1999 (\$0.98 billion) and 2005 (\$1.02 billion), there was a marked increase in the percentage of this spending that was devoted to direct-to-consumer advertising, from 3.3% (\$32.00 million) to 12.0% (\$122.00 million).<sup>25,26</sup> Improving public attitudes toward seeking mental health care in general,<sup>4</sup> increasing rates of treatment in individuals with major depression,<sup>27</sup> and growing public acceptance of a bio-

logic cause of depression<sup>28</sup> may also have contributed to increasing antidepressant use.

Not only are more US residents being treated with antidepressants, but also those who are being treated are receiving more antidepressant prescriptions. Given widespread concerns about early or premature discontinuation of antidepressant treatment,<sup>29,30</sup> this trend may signal improvement in continuity of antidepressant treatment.<sup>31</sup> The clinical and economic reasons for this increase are unclear. Because this trend extended to all broad classes of antidepressants including tricyclic antidepressants, it does not seem to be a function of improved tolerability of the newer antidepressants. Some treated groups including young persons, older adults, Hispanics, and uninsured persons did not experience an increase in the number of antidepressant prescriptions.

The rate of antidepressant use among individuals treated for anxiety, depression, and adjustment disorders increased during the study period. Against the background of increasing antidepressant use, the efficacy of antidepressants has recently come under renewed scrutiny. In the treatment of adult depressive disorder, which remains the most widely studied and well-established clinical indication for antidepressant use, publication bias may have resulted in overstatement of the clinical benefits of antidepressants.<sup>32</sup> A recent pooled analysis of clinical trials suggests that evidence of antidepressant efficacy is largely confined to individuals with severe depression.<sup>33</sup> Second antidepressant trials of initial treatment nonresponders, however, may substantially increase the percentage of depressed adults who respond to treatment with antidepressants.<sup>34</sup> In this regard, it is interesting that the percentage of antidepressant users treated for a depressive disorder remained virtually unchanged during the study decade.

Concern has been expressed that antidepressant use in the community is not efficiently focused on those mostly likely to benefit.<sup>35,36</sup> Results of the present study provide insufficient information about the clinical appropriateness of antidepressant use. For example, the trend toward a decreasing percentage of antidepressant users with unfavorable self-perceived mental health may reflect either increasing effectiveness of antidepressant treatment or expanding antidepressant use by individuals with less symptomatic disorders. One possible area of concern is the persistently high percentage of US residents treated for bipolar disorder who received antidepressants (52.23% in 1996 and 65.35% in 2005). In patients with rapid-cycling bipolar disorder treated with mood stabilizers, 1 randomized, placebo-controlled, double-blind trial, which was published after the 1996-2005 study period, found that antidepressants do not seem to improve recovery, relapse, mood switching, or treatment discontinuation,<sup>37</sup> and some research links antidepressants in patients with rapid-cycling bipolar disorder to more frequent mood episodes.<sup>38</sup> Guidelines suggest that if antidepressants are used in treating bipolar depression, they should be used cautiously and always in combination with antimanic medications.<sup>39</sup>

Only a small minority of patients prescribed antidepressants are treated by a psychiatrist or psychologist during the course of 1 year, and a declining percentage un-

dergo psychotherapy. In a recent report, in the United States, adults treated with antidepressants in 2001-2003 were less likely than those treated in 1990-1992 to have seen a psychiatrist in the last year.<sup>9</sup> Low levels of specialty mental health care among antidepressant users indicate the extent to which antidepressant treatment has become broadly accepted in the general medical sector. Given that roughly 1 in 8 patients (13%) treated with antidepressants by nonpsychiatrist physicians are also treated with antipsychotics or mood stabilizers of proved or unproved efficacy, the results highlight the importance of determining the safety and effectiveness of more complex pharmacologic regimens in general medical settings.

During the study period, patients treated with antidepressants became less likely to undergo psychotherapy. Although depressed patients sometimes prefer psychotherapy over antidepressants,<sup>40</sup> financial factors including out-of-pocket costs to patients<sup>41</sup> and comparatively low third-party clinician reimbursement for psychotherapy<sup>42</sup> have likely led to declining use of psychotherapy.<sup>43</sup> It is also possible that changes in patient perceptions<sup>28</sup> of the effectiveness of antidepressants may have been a factor.

Antidepressant treatment in African Americans and Hispanics in 2005 was less than half the rate in non-Hispanic whites. Similar racial/ethnic differences in antidepressant use have been reported in adult community samples<sup>8</sup> and in adults treated for depression in office-based practice<sup>44</sup> and in the Medicaid program.<sup>45</sup> Several economic, cultural, and social factors have been hypothesized to account for these differences including racial/ethnic variation in mental health service access and availability, educational factors, trust of mental health services, and treatment acceptability.<sup>46</sup> In a study of depressed adult primary care patients, African Americans and to a lesser extent Hispanics were significantly less likely than non-Hispanic whites to believe that medications are effective in treating depression.<sup>47</sup>

Antidepressant use did not significantly increase in African Americans. This is consistent with a broad recent trend toward increasing disparities between African Americans and non-Hispanic whites in mental health service use.<sup>48</sup> More specifically, African Americans may be less predisposed than Hispanics or non-Hispanic whites to use antidepressants. In a sample of primary care patients with depression, African Americans compared with Hispanics or non-Hispanic whites reported a stronger preference for counseling over medication.<sup>49</sup> In a community sample of older adults with depressive symptoms, Hispanics and non-Hispanic whites were also more likely than African Americans to report antidepressant use.<sup>50</sup> Much remains to be learned about the roles of culturally mediated beliefs, attitudes, and social norms<sup>47</sup> and physician factors<sup>51</sup> in shaping racial/ethnic trends in antidepressant use.

The rate of antidepressant treatment in uninsured individuals, although it increased during the study period, also continued to lag well behind that of privately and publicly insured persons. Substantial barriers persist in the provision of mental health care to the 47 million persons in the United States who do not have health insurance.<sup>52</sup>

In October 2004, the US Food and Drug Administration issued a "black box" warning that antidepressants

pose significant risks of suicide in children and adolescents.<sup>53</sup> Despite concern that this warning might result in an excessive decline in antidepressant prescribing, thereby putting depressed and anxious youths at increased risk,<sup>54-56</sup> the present results indicate that the national rate of growth of antidepressant treatment in children and adolescents between 1996 and 2005 closely paralleled its growth in young adults, although the absolute rate remained considerably lower in youths than in young adults, and trends may change in more recent years.

This study is constrained by several limitations in the survey data. First, the MEPS collect data from household informants who may not be fully aware of all of the services used by household members. Stigma and recall problems pose threats to reporting and classifying survey data. Second, it is impossible to determine whether patients who received antidepressant medications actually met diagnostic criteria for recognized clinical indications for antidepressants. However, the large percentage of antidepressant users without clinical mental disorder diagnoses suggests that many US residents are receiving these medications to treat poorly defined conditions. Third, it is impossible to disentangle cause from effect in the increased antidepressant use among respondents with more favorable self-rated mental health. Fourth, several important groups including homeless individuals, nursing home residents, inmates in correctional facilities, and those in other institutional settings are not represented in the national surveys. Fifth, incomplete response to the MEPSs, especially in 2005 (61.3%), may introduce selection bias. However, separate weighting adjustments were performed to reduce bias in survey estimates associated with nonresponse in sampled households and associated with attrition at the person level across survey rounds.<sup>57</sup> Evaluations provide no evidence of nonresponse bias.<sup>57-59</sup> Sixth, because the 1996 MEPS did not classify providers by physician specialty, we are unable to examine trends in treatment provided by psychiatrists from that provided by other physicians.

There was marked growth from 1996 to 2005 in antidepressant treatment in the United States, continuing a trend that started in the late 1980s with the introduction of fluoxetine.<sup>60</sup> Significant increases were evident in many sociodemographic groups but not in African Americans. Among those receiving antidepressants, the likelihood of co-treatment with antipsychotic medications increased, whereas psychotherapy declined. These trends vividly illustrate the extent to which antidepressant treatment has gained acceptance in the United States and the growing emphasis on pharmacologic rather than psychologic aspects of care.

**Submitted for Publication:** September 29, 2008; final revision received November 26, 2008; accepted December 22, 2008.

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**Financial Disclosure:** During the last 5 years, Dr Olfson has received research support from the National Insti-

tutes of Health (NIH); the Agency for Healthcare Research and Quality; the American Foundation for Suicide Prevention; the National Association for Research on Schizophrenia and Affective Disorders; the New York State Office of Mental Health; AstraZeneca, PLC; Bristol-Myers Squibb Co; Eli Lilly and Company; and Ortho-McNeil Janssen Scientific Affairs, LLC; and has worked as a consultant for AstraZeneca, PLC, and Ortho-McNeil Janssen Scientific Affairs, LLC. During the last 5 years, Dr Marcus has received research support from the NIH; the National Patent Safety Foundation; Bristol-Myers Squibb Co; Eli Lilly and Company; AstraZeneca, PLC; and Ortho-McNeil Janssen Scientific Affairs, LLC. **Funding/Support:** This study was supported by grant U18-HS016097 from the Agency for Healthcare Research and Quality and by the National Alliance for Research on Schizophrenia and Depression.

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