

National Patterns of Medication Treatment for Depression, 1987 to 2001

Randall S. Stafford, M.D., Ph.D.; Ellen A. MacDonald, B.S.;
and Stan N. Finkelstein, M.D.

Background: We investigated trends in antidepressant use, as well as broader changes in depression treatment, following the availability of selective serotonin reuptake inhibitors (SSRIs).

Method: Using data from the National Disease and Therapeutic Index, a nationally representative survey of U.S. office-based physicians conducted by IMS HEALTH, we analyzed trends in antidepressant prescribing patterns from 1987 through the third quarter of 2001. Annual sample sizes of physician visits by patients reported to have depression ranged from 3901 visits in 1987 to 6639 in 1998. Outcomes examined included the frequency of depression visits, the likelihood of antidepressant therapy, and the use of specific medications.

Results: The estimated national number of physician visits by patients with depression increased from 14.4 million visits in 1987 to 24.5 million in 2001 (annualized). The rate of antidepressant medication treatment in these patients also increased from 70% in 1987 to 89% in 2001. In 1987, tricyclic antidepressants were prescribed to 47% of patients with depression. The most common individual antidepressants were amitriptyline (14%), trazodone (12%), doxepin (8%), and desipramine (6%). In 1989, a year after its introduction, fluoxetine was prescribed to 21% of patients with depression. The introduction of other SSRIs led aggregate SSRI use to grow to 38% in 1992, 60% in 1996, and 69% in 2000. In 2001, sertraline (18%), paroxetine (16%), fluoxetine (14%), citalopram (13%), and bupropion (9%) were the leading antidepressants, while tricyclics were used in only 2% of patients. The use of benzodiazepines in depression declined from 21% of patients in 1987 to 8% in 2001.

Conclusion: The increasing therapeutic dominance of SSRIs may have contributed to other changes in depression treatment, including declining benzodiazepine use, increased aggregate antidepressant treatment rates, and increased reporting of depression.

(Primary Care Companion J Clin Psychiatry 2001;3:232-235)

Received Nov. 13, 2001. From the Institute for Health Policy, Massachusetts General Hospital/Harvard Medical School, Boston (Dr. Stafford and Ms. MacDonald); Program on the Pharmaceutical Industry, Massachusetts Institute of Technology, Cambridge, Mass. (Dr. Finkelstein); and the Stanford Center for Research in Disease Prevention, Stanford University, Palo Alto, Calif. (Dr. Stafford).

This study was supported by the Massachusetts General Hospital Primary Care Operations Improvement Initiative.

Dr. Finkelstein is a consultant for Medstat Group and has received grant/research support from Merck, Wyeth-Ayerst, and Pfizer. Dr. Stafford and Ms. MacDonald have no affiliation or relationship to report relevant to the subject matter in this article.

The authors thank IMS HEALTH, Plymouth Meeting, Pa., for providing the data used in their analysis.

Corresponding author and reprints: Randall S. Stafford, M.D., Ph.D., Stanford Center for Research in Disease Prevention, Stanford University, Palo Alto, CA 94304 (email: rstafford@stanford.edu).

Depression affects more than 19 million adults in the United States annually.¹ In 1990, major depression was the fourth ranked cause of disability and premature death in the United States, as well as worldwide.² Recent studies have shown depression to be a major risk factor for a range of chronic medical conditions, as well as for increased mortality.³⁻⁶ For the United States in 1990, it was estimated that \$30.4 to \$43.7 billion in direct and indirect costs was attributable to depression.^{7,8}

Depression can be effectively treated with medications. Between 65% and 75% of patients will improve with adequate antidepressant pharmacotherapy.⁹ Currently, there are 3 major categories of antidepressant medications: tricyclic and related cyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and other antidepressant compounds. In the past, monoamine oxidase inhibitors (MAOIs) also were used. Among these medications, SSRIs have the most favorable side effect and safety profiles, characteristics likely to increase their prescription by physicians and continued use by patients.^{10,11} Historically, anxiolytics such as the benzodiazepines have also been prescribed for depression, although they are indicated most clearly for the treatment of anxiety.¹²

Past studies have documented several changes in antidepressant prescribing patterns over time, including an increasing number of outpatient visits associated with psychotropic medications. For example, the percentage of visits associated with psychotropic medications increased from 5.1% in 1985 to 6.5% in 1994.¹³ This increase was

particularly pronounced among visits to psychiatrists. Associated with this change were the introduction and increasing use of SSRIs, beginning in 1988. Changes in prescribing practices were most pronounced for patients with less severe disorders.¹⁴ Trends in the late 1990s suggested the increasing dominance of SSRIs compared with TCAs and other antidepressants.¹⁵ As late as 1996, benzodiazepines remained a prominent feature of depression treatment.¹⁵

Using national data on physician prescribing patterns between 1987 and 2001, we investigated recent trends in antidepressant use and other aspects of depression treatment that have occurred following the introduction of SSRIs.

METHOD

Data for this study came from the National Disease and Therapeutic Index (NDTI), a continuing physician survey conducted by IMS HEALTH (Plymouth Meeting, Pa.). The NDTI provides nationally representative diagnostic and prescribing information on patients treated by office-based physicians in the United States. A random sample of office-based physicians stratified by specialty is selected from the masterlists of the American Medical Association (Chicago, Ill.) and the American Osteopathic Association (Chicago, Ill.). This sample is used to generate extrapolations to national practice patterns.¹⁶ Among the approximately 3500 participating physicians, 2 consecutive workdays per quarter are selected for data collection.

Physicians provide information on each patient contact during their 2-day data collection period. Physician contacts with patients with depression are largely composed of office visits. For example, in 2001, 92% of contacts were office visits, while 4% were telephone calls and 2% were nursing home visits. Each patient diagnosis generates a separate diagnosis record on which the physician records information on specific new or continuing medication therapies provided for the condition. A single patient contact may generate multiple diagnosis records, each of which may list multiple medications. On the other hand, diagnosis records may also list no medications if none were being employed for the specific condition. Medication reporting reflects the physician's best knowledge of new or continuing prescription and nonprescription medications taken by each patient. The NDTI does not capture information on patient adherence or unreported self-medication.

Using NDTI reports from 1987 through the third quarter of 2001, we selected visits by patients reported to have depression-related diagnoses. The ICD-9 codes for these diagnoses included depressive disorder not elsewhere classified (ICD-9 311), neurotic depression (ICD-9 300.4), and brief depressive reaction (ICD-9 309.0). Among these, depressive disorder not elsewhere classified accounted

for the vast majority of cases reported (74% in 2001), with neurotic depression accounting for a sizable minority of visits (23% in 2001). Annual sample sizes of depression visits varied from 3901 depression visits in 1987 to 6385 in 2000, with 4829 for the first 3 quarters of 2001. Annual data are presented as the aggregate of the quarterly surveys conducted within each year, except for 2001, for which figures were annualized by inflating drug mention information for quarters 1 through 3 by a factor of four thirds.

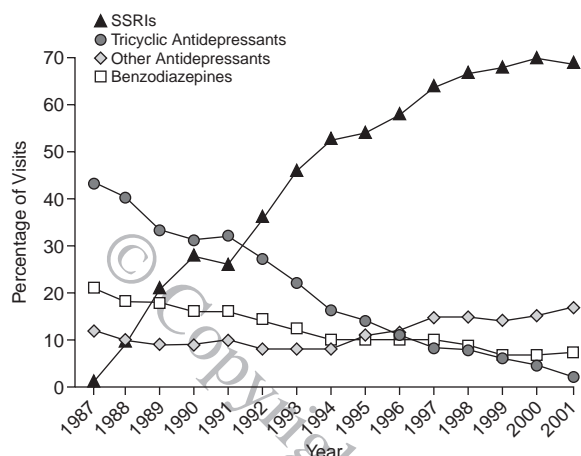
We examined annual prescribing data to assess the proportion of depression visits in which individual medications or medication classes were reported as specific treatments for depression. All reported brand and generic names for those specific compounds with more than 1 listing were combined into a single generic name. We defined medication classes as TCAs, SSRIs, MAOIs, and all other antidepressants. Medication use in these classes is not mutually exclusive because some patients were treated with multiple medications. Limited information was also available on the characteristics of visits, including age, gender, and physician specialty. For the sample sizes available for depression visits, the 95% confidence intervals around our estimates of annual medication usage rates are less than $\pm 1\%$.

RESULTS

Between 1987 and 2001, the estimated national number of visits by patients reported to have depression increased from 14.4 million visits to an annualized 24.5 million, an increase of 70%. Several changes occurred in the composition of these visits. The role of psychiatrists in providing care gradually declined; psychiatrists accounted for 44% of visits in 1987, but only 29% in 2001. The role of primary care physicians increased over this same period (50% in 1987 to 64% in 2001). There also was a decrease in the age of patients, particularly in the proportion of patients 65 years or older (22% in 1987 to 18% in 2001). The proportion of depression visits by women stayed constant at around two thirds through this same time period.

Among patients reported to have depression, the rate of antidepressant medication treatment steadily increased from 70% of patients in 1987 to 76% in 1990 to 87% in 1996 to 89% in 2001. The selection of particular antidepressants changed dramatically over this time period. In 1987, tricyclic antidepressants (TCAs) were the predominant drug class prescribed to patients with depression. Physicians reported the use of a TCA in 47% of visits by patients with depression, with amitriptyline (14% of depression patients), doxepin (7.7%), and desipramine (6.3%) the most commonly prescribed TCAs. Trazodone was the most common non-TCA antidepressant reported in 1987 (12%).

Figure 1. National Trends in Antidepressant and Benzodiazepine Use in Depression^a



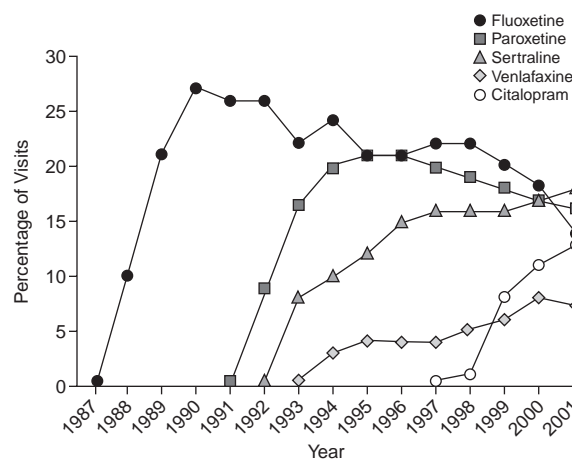
^aData from IMS HEALTH, National Disease and Therapeutic Index, January 1987 through September 2001. Data for 2001 were estimated by annualizing data through the third quarter of that year. Abbreviation: SSRI = selective serotonin reuptake inhibitor.

The introduction of fluoxetine as the first SSRI in January 1988 drastically changed antidepressant prescribing patterns. During the first year fluoxetine was on the market, 9.7% of patients with depression received this drug. In 1989, 1 year after its introduction, fluoxetine was prescribed to 21% of patients with depression. The introduction of sertraline in 1992 and paroxetine in 1993 led aggregate SSRI use to increase to 46% of depression patients by 1993. Subsequent release of venlafaxine in 1994, fluvoxamine in 1995, and citalopram in 1998 increased SSRI use still further to 53% in 1994, 64% in 1997, and 69% in 2001 (Figure 1). While fluoxetine use remained at nearly a quarter of patients through the mid-1990s, use of it fell in the late 1990s. In 2001, sertraline (18%), paroxetine (16%), fluoxetine (14%), and citalopram (13%) were the most commonly prescribed antidepressants (Figure 2).

With increasing SSRI use, the frequency of use of other classes of antidepressants has declined. In particular, TCA use has steadily declined from 47% in 1987 to 22% in 1992 to 11% in 1996 to 2.1% in 2001. Among TCAs in 2001, amitriptyline (1.5%) remains the most commonly prescribed. Throughout the 1987 to 2001 time period, the use of MAOIs has remained at a very low level (1.0% in 1987 and < 0.1% in 2001). The use of antidepressants in other classes has increased slightly over time, from 12% in 1987 to 17% in 2001. Among this heterogeneous group of medications, trazodone (12%) was the dominant medication in 1987. In 2001, bupropion (8.5%), nefazodone (3.6%), and trazodone (2.6%) were the most common other antidepressants.

In 1987, benzodiazepines were used for the specific purpose of treating depression in 21% of depression patients. This number decreased steadily to 10% in 1994 and

Figure 2. National Trends in Selective Serotonin Reuptake Inhibitor Use in Depression^a



^aData from IMS HEALTH, National Disease and Therapeutic Index, January 1987 through September 2001. Data for 2001 were estimated by annualizing data through the third quarter of that year.

7.5% in 2001, a decrease of 64% from 1987. The most commonly prescribed individual benzodiazepines in 1987 were alprazolam (9.2% of depression visits), lorazepam (2.9%), and diazepam (2.5%). In 2001, use of each of these medications had fallen (alprazolam, 3.1%; lorazepam, 1.7%; and diazepam, 0.5%).

DISCUSSION

Our analysis of trends in depression treatment suggests that tremendous alterations have occurred following the introduction of SSRIs. As new SSRIs have been released, the prominence of SSRIs has continued to grow to the point that their use was reported in 69% of depression visits in 2001. Coincident with growing SSRI use, there has been an increasing number of depression visits and an increasing likelihood of antidepressant therapy at these visits. As a result, the number of antidepressant prescriptions increased by 116% between 1987 and 2001. Throughout this period, the use of benzodiazepines has decreased from 21% in 1987 to 7.5% in 2001.

While the increasing dominance of SSRIs has been documented in the past,¹³⁻¹⁵ our results differ from past results in indicating the increasing heterogeneity of antidepressant drugs. With the addition of other SSRIs, fluoxetine is no longer as dominant a medication as it was through the mid-1990s. In 2001, the use of fluoxetine was surpassed by the use of both sertraline and paroxetine.

The increase in the frequency of depression visits that we noted may be due to multiple interrelated factors, including increasing physician detection of depression, increasing patient willingness to seek care for depression, and an increasing perception that effective and tolerable

therapy is available. The advent of SSRIs may have contributed to these patterns, in particular because of their favorable side effect and safety profiles.

The dramatic shift away from benzodiazepine use for depression is notable. There may be many contributors to this trend, including increasing evidence suggesting a limited role for benzodiazepines as a treatment for depression. The broader indications of SSRIs, including their use for anxiety disorders, may have helped decrease benzodiazepine use in patients with anxiety symptoms along with depression.

A number of possible limitations of our analysis should be noted. Our population of patient visits was based on physician reporting of depression. This reporting may differ from patients' objective signs and symptoms of depression. Rates of antidepressant use rely on physician reporting of medications at patient visits and do not account for patient nonadherence. Each NDTI count reflects a single patient visit with a physician, at which the named medication was prescribed. These visit-based data may overestimate medication use by oversampling those patients who make frequent visits to physicians. Finally, we are unable to determine the specific causes of the observed trends in SSRI use, although these causes quite likely include drug characteristics, physician and public perceptions, and pharmaceutical promotion.

Even with these potential limitations, the figures obtained from NDTI are consistent with those of the National Ambulatory Medical Care Survey (NAMCS), a federal, public-use data source employed in many past assessments of national antidepressant use. For example, SSRI use was noted to be 3 times that of TCAs in 1995 for both the NDTI and NAMCS data sources.¹⁵

Substantial changes in the management of depression occurred between 1987 and 2001. The increasing therapeutic dominance of SSRIs may have contributed to other changes in depression treatment. Perhaps because of the side effect profiles and perceived effectiveness of SSRIs,

increasing SSRI use may also have contributed to the declining use of benzodiazepines, increased aggregate antidepressant treatment rates, and increased physician visits for depression.

REFERENCES

1. Regier DA, Narrow WE, Rae DS, et al. The de facto US mental and addictive disorders service system: epidemiologic catchment area prospective 1-year prevalence rates of disorders and services. *Arch Gen Psychiatry* 1993;50:85–94
2. Judd LL. The clinical course of unipolar major depressive disorders. *Arch Gen Psychiatry* 1997;54:989–991
3. Musselman DL, Evans DL, Nemeroff CB. The relationship of depression to cardiovascular disease: epidemiology, biology, and treatment. *Arch Gen Psychiatry* 1998;55:580–592
4. Januzzi JL Jr, Stern TA, Pasternak RC, et al. The influence of anxiety and depression on outcomes of patients with coronary artery disease. *Arch Intern Med* 2000;160:1913–1921
5. Wulsin LR, Vaillant GE, Wells VE. A systematic review of the mortality of depression. *Psychosom Med* 1999;61:6–17
6. Wulsin LR. Does depression kill? [letter]. *Arch Intern Med* 2000;160:1731–1732
7. Rice D, Miller LS. The economic burden of affective disorders. In: Scheffler RM, Rossiter LF, Hu T-W, eds. *Advances in Health Economics and Health Services Research*. Greenwich, Conn: JAI Press Inc; 1993
8. Greenberg PE, Stiglin LE, Finkelstein SN, et al. The economic burden of depression in 1990. *J Clin Psychiatry* 1993;54:405–419
9. Bhatia SC, Bhatia SK. Major depression: selecting safe and effective treatment. *Am Fam Physician* 1997;55:1683–1698
10. Vanderhoff BT, Miller KE. Major depression: assessing the role of new antidepressants. *Am Fam Physician* 1997;55:249–254, 259–260
11. Guze BH, Gitlin M. New antidepressants and the treatment of depression. *J Fam Pract* 1994;38:49–57
12. American Psychiatric Association. Practice Guideline for Major Depressive Disorder in Adults. *Am J Psychiatry* 1993;150(suppl 4):1–26
13. Pincus HA, Tanielian TL, Marcus SC, et al. Prescribing trends in psychotropic medications: primary care, psychiatry, and other medical specialties. *JAMA* 1998;279:526–531
14. Olfson M, Marcus SC, Pincus HA, et al. Antidepressant prescribing practices of outpatient psychiatrists. *Arch Gen Psychiatry* 1998;55:310–316
15. Stafford RS, Misra B, Ausiello JC, et al. National patterns of depression treatment in primary care. *Primary Care Companion J Clin Psychiatry* 2000;2:211–216
16. Munnangi S, Sonnenberg A. Time trends of physician visits and treatment patterns of peptic ulcer disease in the United States. *Arch Intern Med* 1997;157:1489–1494