

Frequency of Follow-up Care for Adult and Pediatric Patients During Initiation of Antidepressant Therapy

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Objectives: To measure the timing and frequency of follow-up care during the initiation phase of antidepressant therapy, and to compare the typical pattern of care with current product guidelines.

Study Design: Retrospective cohort study.

Methods: The study included 84 514 adult and pediatric patients who started a new course of antidepressant therapy for any indication between July 2001 and September 2003. Patients were members of a large managed care organization in the northeastern United States. Ambulatory visits during the first 12 weeks of treatment were identified using medical claims data. Outcome measures were time to first follow-up visit, frequency of follow-up visits, and percentage of patients receiving recommended levels of care.

Results: During the first 4 weeks of treatment with antidepressants, only 55.0% of patients saw a healthcare provider for any purpose, and only 17.7% saw a provider for mental healthcare. Ambulatory visit rates during the first 4, 8, and 12 weeks were significantly lower than the minimum levels recommended in product labeling ($P < .0001$). Only 14.9% of patients received the Food and Drug Administration–recommended level of follow-up care during the first 4 weeks, 18.1% at 8 weeks, and 22.6% at 12 weeks.

Conclusions: Adults and children who begin a new course of antidepressant therapy tend to receive far less monitoring than is recommended in current product labeling. Given safety concerns during the initiation phase, earlier and more frequent follow-up care appears desirable. Further research is needed to identify the most cost-effective schedule of care.

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In October 2004, the Food and Drug Administration (FDA) directed manufacturers to include a new “black box” warning and expanded warning sections in the labeling for all antidepressant products.¹⁻³ The new labeling warns healthcare providers about the increased risk of suicidal thoughts and actions (“suicidality”) in children and adolescents who take antidepressant medications for any indication, including major depressive disorder and obsessive-compulsive disorder (OCD). The FDA also developed a patient medication guide on the risk of suicidality and the precautions that can be taken by patients, parents, and caregivers.^{2,4} These regulatory actions were based on a combined analysis of adverse events in 24 clinical trials

that studied the use of antidepressant drugs in pediatric populations. When results were pooled across all drugs and all indications, the analysis showed a small but statistically significant increase in suicidality risk for antidepressants (compared with placebo) during the first few months of treatment.^{5,6}

The new warning labels advise healthcare providers to monitor pediatric patients closely for signs of clinical worsening, suicidality, or unusual changes in behavior, especially during the first few months of a new course of antidepressant therapy or after a change in dose.³ The warning labels recommend a specific pattern of follow-up care: at least weekly face-to-face visits during the first 4 weeks of treatment, visits every other week during the next 4 weeks, a visit at 12 weeks of treatment, and visits as indicated clinically beyond that point. Additional contacts by telephone as needed are encouraged between the face-to-face visits. More concentrated monitoring during the early stages of treatment is recommended because there is some evidence that the risk of suicidality may be higher during the first few weeks of treatment.⁷

Although the risk of suicidality in children and adolescents has been the primary focus of public and regulatory attention, the FDA also has begun to address the possibility of an increased risk of suicidality in adult users of antidepressants.^{1,8,9} Warnings about this risk were first introduced into the labeling of selected products in March 2004, and they were expanded and applied to all antidepressant products in October 2004.^{1,8} The new product labels recommend “close monitoring” of adult patients for signs of clinical worsening or suicidality, especially during the first few months of a new course of therapy for depression, and they recommend an intensive pattern of follow-up visits similar to the pattern recommended for pediatric care.³

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In June 2005, the FDA announced that it had begun a comprehensive analysis of adult clinical trial data (similar to the combined analysis of pediatric trial data) in an effort to create a stronger evidentiary basis for future regulatory actions in this area.⁹

The new suicidality warnings build on a broader framework of clinical practice guidelines for the use of antidepressants in the treatment of depression, anxiety disorders, and other conditions. These guidelines have been developed most extensively for the treatment of depression in adults,¹⁰⁻¹⁶ whereas relatively few have been developed for the pharmacological treatment of anxiety disorders¹⁷⁻¹⁹ or for pediatric use of antidepressants for any indication. Guidelines for the treatment of depression call for close monitoring of patients during the acute phase of treatment, which generally lasts a few months and ends with remission of symptoms.^{10,11} The primary goals of monitoring are to assess the effectiveness of therapy, identify side effects, monitor the patient's condition, adjust therapy as needed, and promote adherence.¹⁰⁻¹² Guidelines for the treatment of anxiety disorders also call for close monitoring of patients who receive medication therapy.¹⁷⁻¹⁹

Guidelines vary widely in the recommended frequency and timing of follow-up visits for patients who begin a new course of antidepressant therapy. The American Psychiatric Association recommends a vigorous schedule of monitoring during the acute phase of treatment for depression—at least weekly contacts in routine cases and multiple contacts per week in more complex cases.¹⁰ Monitoring contacts are defined broadly to include face-to-face visits, telephone contacts, or contacts with other knowledgeable clinicians, depending on the circumstances.¹⁰ In an earlier set of guidelines, the Agency for Health Care Policy and Research recommended face-to-face visits every 10 to 14 days during the first 6 to 8 weeks of treatment for patients with less severe depression, and weekly visits in more severe cases.¹¹ Other clinical guidelines recommend follow-up contacts on a weekly, biweekly, or monthly basis, depending on a variety of factors.¹²⁻¹⁶ The FDA guidelines fall roughly in the middle of this range—weekly face-to-face visits during the first month, tapering to monthly face-to-face visits by the third month.

Many studies have examined patterns of treatment response to antidepressant medications, but only a few have reported data on the typical frequency of follow-up visits for adult or pediatric patients who initiate antidepressant therapy in usual practice.²⁰⁻²⁴ The limited available data suggest that follow-up visit rates tend to be low,^{21,23,24} but none of these studies provide a direct measure of the concordance between usual practice and

the new FDA guidelines. The most commonly used measure of visit frequency was developed by the National Committee for Quality Assurance to assess the pharmacological management of depression.^{21,25} As defined in Health Employer Data and Information Set (HEDIS) specifications, “optimal practitioner contact” frequency is a minimum of 3 follow-up visits for mental healthcare during the first 12 weeks of a new treatment episode; at least 2 of the measured visits must be face-to-face, and 1 may be a telephone contact.²⁵ This metric is useful for evaluating the overall quality of care, but it is not well suited to measuring the concordance of current practice with the new FDA guidelines for antidepressant products. The HEDIS metric is limited to patients with depression (rather than any condition treated with antidepressants), it provides no information on the follow-up care received by pediatric patients (because the metric is defined only for adults), and it provides no information on the time course of visits during the first 12 weeks of care. Without more comprehensive benchmark data, it is difficult to gauge whether the pattern of care defined in the new product labeling is feasible and realistic in the context of current practice.

The objectives of this study were to measure the timing and frequency of follow-up visits during the initial phase of antidepressant therapy, and to compare the typical pattern of care with the pattern recommended in product labeling. The design of the study mirrored the scope and content of the new FDA guidelines. The study measured the time course of face-to-face visits for any patient (adult or pediatric) who began using an antidepressant medication for any treated condition, and it compared the typical pattern of visits with the time course recommended in product guidelines. Although the new guidelines apply equally to all pediatric users, we measured visit frequency separately for 3 pediatric age groups (0-6 years, 7-12 years, and 13-18 years), because of the wide variations in treated conditions and incidence of use across these groups.

METHODS

Study Population

Patients were participants in medical and pharmacy benefit plans administered by a large managed care organization in the northeastern region of the United States; the medical plans included coverage for mental healthcare. The study population included all plan participants who had combined eligibility for medical and pharmacy benefits at any time during the study period, which extended from January 1, 2001, through

December 31, 2003. A total of 2 411 316 plan participants met the criteria for inclusion.

Medical utilization data (including mental health claims data) were drawn from an administrative claims database maintained by the managed care organization. Drug utilization data were drawn from a prescription claims database maintained by Medco Health Solutions, Inc, the pharmacy benefits management company that manages the prescription benefit plans for this population. Medical and pharmacy claims data were integrated at the patient level; personal identifying information was not retained.

Patient Identification

Patients were initially identified for the study sample if they filled a prescription for an antidepressant during an identification period that extended from July 1, 2001, through September 30, 2003. Prescriptions for all classes of antidepressants were included in the analysis (see the **Appendix** available online at www.ajmc.com). A prescription was considered the start of a *new episode* if no antidepressant prescriptions had been filled for the same patient during the prior 180 days (a 6-month negative medication history). The *index date* for the new episode was the fill date of the prescription at the start of the episode. Patients were included in the final study sample if they had continuous benefits eligibility during the 6 months before the index date and the 3 months after the index date. A total of 84 514 patients with new episodes of antidepressant therapy met the criteria for inclusion in the study sample. A small percentage of patients (4.9%) had 2 or more new episodes during the identification period; these recurrent episodes were included in the final study sample. As defined here, a new episode is a new course of therapy for any condition treated with antidepressants; this definition accords with the scope of the new warning labels for these products.

Data Collection

For each patient in the study sample, medical claims were used to track ambulatory follow-up care during a 12-week analysis period after the index date of the new episode. Ambulatory care included office visits and outpatient visits; telephone visits were not included. Follow-up visits were identified at 2 levels of specificity: all ambulatory visits and mental health visits.

All Ambulatory Visits. Ambulatory visits were identified by place-of-service codes for office and outpatient visits (Appendix). All visits were included, no matter what diagnostic coding was used in billing. This measure provides an upper bound for follow-up visits where the patient's response to antidepressant therapy may have been addressed. All face-to-face visits provide an oppor-

tunity for follow-up care, even if the visit was scheduled or coded for another purpose.

Mental Health Visits. Mental health visits were identified by Current Procedural Terminology (CPT) codes for evaluation and management visits in conjunction with mental health diagnostic codes, or by CPT codes for psychiatric visits (Appendix). This measure provides a lower bound for follow-up visits where the patient's response to antidepressant therapy was likely addressed. The measure is likely to underestimate the actual number of follow-up visits, because some mental health visits may not be coded as such.

For each patient starting a new episode of therapy, the patient's age and sex were derived from an eligibility database maintained by the managed care organization. Patient age was measured at the index date of the new episode.

Outcome Measures

Analyses were conducted separately for children (age ≤18 years) and adults (age ≥19 years). For each age group, 3 sets of measures were derived from the claims data:

- *Time to first visit.* The percentage of patients who had at least 1 follow-up visit during a specified interval after the start of a new episode. This percentage was measured at 1, 2, 3, 4, 8, and 12 weeks after the index date.
- *Frequency of visits.* The average number of follow-up visits during specified intervals after the start of therapy. The frequency was measured at 4, 8, and 12 weeks after the index date.
- *FDA-recommended level of care.* The percentage of patients who received the minimum level of follow-up care recommended in product labeling—at least 4 visits in the first 4 weeks, at least 6 visits in the first 8 weeks, and at least 7 visits in the first 12 weeks.

Data Analysis

All measures, including exact confidence intervals, were computed using SAS version 8.0 (SAS Institute Inc, Cary, NC).

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RESULTS

Patient Characteristics

The age and sex distribution of patients in the study sample is shown in **Table 1**. Incidence rates for new episodes varied widely as a function of both sex and age. The incidence rate among adults was nearly twice as high for women as for men, but among children 12 years of age and younger, the incidence of new episodes was

Table 1. Characteristics of Patients With New Episodes of Antidepressant Therapy

Characteristic	Children				Adults (19 y and Older)	All Patients
	0-6 y	7-12 y	13-18 y	All (0-18 y)		
Mean age, y	4.6	10.1	15.8	13.9	45.6	43.7
Female, n (%)	55 (32.7)	454 (33.6)	1916 (54.6)	2425 (48.2)	51 830 (65.2)	54 255 (64.2)
Male, n (%)	113 (67.3)	897 (66.4)	1591 (45.4)	2601 (51.8)	27 658 (34.8)	30 259 (35.8)
Study sample, n	168	1351	3507	5026	79 488	84 514
Total population, n	239 658	196 121	168 171	603 950	1 807 366	2 411 316
Incidence rate of new episodes, %	0.1	0.7	2.1	0.8	4.4	3.5

twice as high for boys as for girls. Among adolescents (aged 13-18 years), the incidence rate was higher for girls.

Timing and Frequency of Follow-up Visits

The majority of patients did not have a face-to-face visit with a healthcare provider during the first few weeks after the start of antidepressant therapy (Table 2). During the first week of medication use, only 1 in 4 patients (25.3%) saw a healthcare provider for any purpose, and fewer than 1 in 10 patients (8.0%) saw a healthcare provider for mental health. During the first 4 weeks of treatment, only 55.0% of patients had a face-to-face visit for any purpose, and only 17.7% had a visit for mental healthcare. After 8 weeks and 12

weeks of treatment, many patients still had not had follow-up contact with a healthcare provider (Figure 1).

The cumulative frequency of follow-up visits after the start of antidepressant therapy is shown in Table 3. In general, adult and pediatric patients had only 1 or 2 face-to-face visits with healthcare providers during the first 4 weeks of treatment. During the first 12 weeks, they averaged 4 to 5 face-to-face visits. The observed visit rates were significantly below the minimum levels recommended in product labeling ($P < .0001$ at each interval for all age groups).

The differences between guidelines and practice are illustrated in Figure 2 for adult and pediatric patients combined. The average number of ambulatory visits (for any purpose) fell short of the minimum levels recom-

Table 2. Percentage of Patients Who Had at Least One Face-to-face Visit With a Healthcare Provider During the Specified Interval After the Start of Antidepressant Therapy

Visit Type	Children, %				Adults (19 y and Older), %	All Patients, %
	0-6 y	7-12 y	13-18 y	All (0-18 y)		
Any ambulatory visit during the first:						
1 wk	22.0	27.2	31.6	30.2	25.0	25.3
2 wk	38.1	42.0	45.4	44.2	38.6	38.9
3 wk	49.4	51.7	54.7	53.7	47.5	47.9
4 wk	60.1	60.0	60.7	60.5	54.7	55.0
8 wk	77.4	75.3	74.2	74.6	69.5	69.8
12 wk	83.9	82.3	80.6	81.2	76.8	77.0
Any mental health visit during the first:						
1 wk	4.8	13.8	19.2	17.2	7.5	8.0
2 wk	9.5	21.6	27.6	25.4	11.6	12.4
3 wk	11.3	25.8	33.4	30.6	14.3	15.3
4 wk	14.9	30.4	36.9	34.4	16.7	17.7
8 wk	23.2	38.9	45.3	41.9	21.6	22.8
12 wk	27.4	45.0	48.4	46.8	24.1	25.5

mended in product guidelines, and mental health visits fell far short of the recommended frequency at each interval ($P < .0001$ all comparisons). The average number of visits per month was roughly constant, diminishing only slightly over time. This finding contrasts with the recommendations in product labeling, which call for more frequent visits during the first month of a new episode.

The gaps between recommended care and current practice were corroborated by an analysis of the number of patients who received the FDA-recommended levels of care during the first 12 weeks (Table 4). At each interval after the start of treatment, only a small percentage of patients received follow-up care that met the minimum level defined in product labeling.

Although comparing visit rates across age groups was not a primary objective of this study, some significant differences were observed (Table 3). In general, children had more frequent ambulatory contacts during the first 3 months of antidepressant treatment compared with adults ($P < .05$ at each interval, all children vs all adults). Children had a much greater frequency of mental health visits than adults ($P < .05$ at each interval), because a larger proportion of their ambulatory visits were with mental health professionals. Adolescent patients (aged 13-18 years) tended to receive more frequent follow-up care than younger chil-

dren (aged 0-6 years and aged 7-12 years) during the first 3 months of antidepressant treatment. This pattern was especially strong for mental health visits; adolescent patients had significantly more mental health visits than patients in either of the younger age groups ($P < .05$ at each interval).

DISCUSSION

Clinical practice guidelines recommend frequent follow-up visits with patients who begin a course of anti-

Figure 1. Percentage of Patients Who Had at Least 1 Follow-up Visit After Starting Antidepressant Therapy

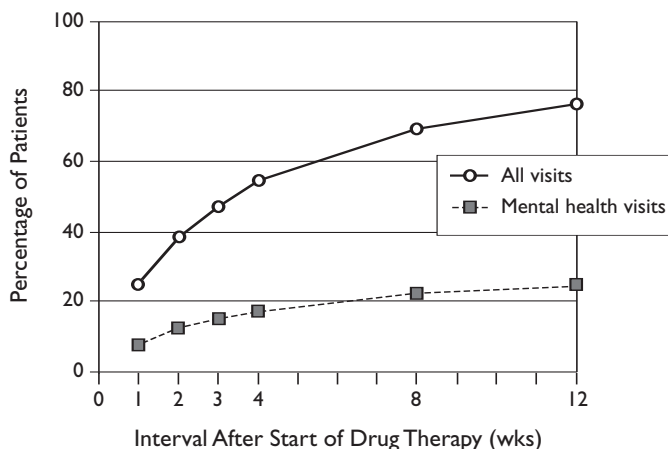
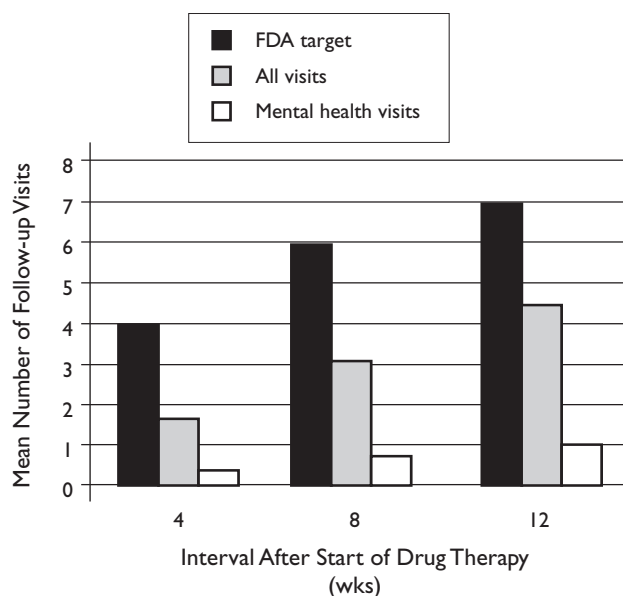


Table 3. Frequency of Face-to-face Visits With Healthcare Providers After the Start of Antidepressant Therapy*

Visit Type	Children				Adults (19 y and Older)	All Patients
	0-6 y	7-12 y	13-18 y	All (0-18 y)		
Ambulatory visits during the first:						
4 wk	1.23 (0.98, 1.49)	1.66 (1.52, 1.79)	1.89 (1.81, 1.98)	1.81 (1.74, 1.88)	1.64 (1.62, 1.66)	1.65 (1.63, 1.66)
8 wk	2.53 (2.09, 3.14)	3.25 (3.01, 3.48)	3.58 (3.43, 3.73)	3.46 (3.33, 3.58)	3.10 (3.06, 3.13)	3.11 (3.09, 3.15)
12 wk	3.76 (3.14, 4.39)	4.70 (4.37, 5.02)	5.10 (4.89, 5.31)	4.95 (4.78, 5.12)	4.45 (4.41, 4.49)	4.48 (4.44, 4.52)
Mental health visits during the first:						
4 wk	0.29 (0.15, 0.43)	0.71 (0.64, 0.79)	0.95 (0.89, 1.00)	0.86 (0.82, 0.91)	0.37 (0.36, 0.38)	0.40 (0.39, 0.40)
8 wk	0.55 (0.34, 0.76)	1.37 (1.23, 1.50)	1.78 (1.69, 1.88)	1.63 (1.55, 1.71)	0.69 (0.68, 0.70)	0.75 (0.73, 0.76)
12 wk	0.82 (0.52, 1.11)	2.03 (1.84, 2.21)	2.52 (2.39, 2.65)	2.33 (2.23, 2.44)	0.97 (0.95, 0.99)	1.05 (1.03, 1.07)

*Values are mean (95% confidence interval). The actual frequency of visits for antidepressant medication management is likely to fall between the frequency of visits coded for mental health (lower bound) and the frequency of all ambulatory visits (upper bound).

Figure 2. Frequency of Face-to-face Visits After the Start of Antidepressant Therapy (All Patients)



FDA indicates Food and Drug Administration.

depressant therapy, and product labels now call for a vigorous schedule of face-to-face visits to monitor for signs of suicidality. The results of our study suggest that follow-up care in practice is far less frequent than what is recommended by the current product labeling. In this study sample, more than 80% of patients had no mental health visits with healthcare providers during the first 4 weeks after starting antidepressant therapy, and the

average patient had only 1 or 2 face-to-face visits for any purpose during that period.

Although FDA guidelines call for vigorous follow-up care for both adults and children who begin using antidepressants, the primary impetus for the new labeling was the risk of increased suicidality in children. A significant increase in suicidality was demonstrated in pediatric studies (when data were pooled across drugs and indications),^{2,5,6} but an association of this type has not yet been demonstrated in combined analyses of adult studies.⁹ In this context, it may be reassuring that children generally receive more frequent follow-up care than adult patients after the initiation of treatment with antidepressants. However, the level of follow-up care for children still falls far short of the close monitoring that is recommended during the first few months of therapy.

The significance of these gaps between guidelines and practice is difficult to assess, because there has been very little research on what patterns of follow-up care are most likely to facilitate recovery or reduce the risk of adverse outcomes. Clinical guidelines on visit frequency are based primarily on professional consensus, because evidence from clinical studies is generally not available.^{10,22} The recommendations developed by the FDA also appear to be based on expert opinion, in response to public and professional appeals for a more precise definition of close monitoring.²⁶ There is some evidence that increased suicidality in children is more likely to occur (if it occurs at all) during the first 9 days after the start of antidepressant therapy, which lends support to the FDA recommendation to schedule more frequent visits during the first few weeks of treatment.^{2,7} However, there is no published evi-

Table 4. Percentage of Patients Who Received the FDA-recommended Level of Follow-up Care After the Start of Antidepressant Therapy

Standard of Care	Visit Measure	Children, %				Adults (19 y and Older), %	All Patients, %
		0-6 y	7-12 y	13-18 y	All (0-18 y)		
At least 4 visits during the first 4 wk	All visits	6.6	15.1	18.9	17.4	14.7	14.9
	Mental health visits	2.4	5.9	9.2	8.1	3.1	3.4
At least 6 visits during the first 8 wk	All visits	12.5	19.7	24.2	22.6	17.8	18.1
	Mental health visits	3.0	8.2	12.3	10.9	4.2	4.6
At least 7 visits during the first 12 wk	All visits	17.3	25.2	29.0	27.6	22.2	22.6
	Mental health visits	3.0	11.4	15.3	13.8	5.3	5.8

FDA indicates Food and Drug Administration.

dence that frequent visits during this period will reduce the risk of suicidal thoughts or actions, and it may be unrealistic to look for evidence of that kind in the near term. The associations between antidepressant use and increased suicidality are somewhat fragile statistically; for some drug classes, medical conditions, and outcome measures, the associations are not statistically significant in pooled analyses.^{5,27-29} Given the measurement challenges, it may be difficult to test whether a particular regimen of follow-up care improves the detection of suicidality or reduces the risk of self-harm.

Although the risk of suicidality is the primary focus of the new warning labels, the clinical rationale for close monitoring during the initial phase of antidepressant therapy is much broader in scope. Follow-up care is designed to assess the patient's response to treatment and adjust medications as needed to optimize the likelihood of recovery. Management of side effects is an important component of follow-up care, because adverse reactions may lead to poor compliance or therapy discontinuation, increasing the risk of treatment failure.^{10,11,13,30} It is widely assumed that more frequent face-to-face visits will improve compliance, thereby increasing the likelihood of recovery, but there is very little direct evidence for this.^{10,22} In a comparison of usual care with guidelines-based care for depression, researchers found that patients with weekly or biweekly acute-phase visits had significantly better outcomes than patients with less frequent visits^{31,32}; however, these results may have been confounded by other differences in treatment. In the absence of strong research support, the linkage between increased visit frequency and improved outcomes remains largely intuitive.

The new product labeling endorses the use of telephone contacts with patients, parents, or caregivers as a supplemental form of patient monitoring.³ Telephone contacts are a cost-effective way to evaluate a patient's status between face-to-face visits, and systematic use of telephone interventions can improve outcomes for patients with depression.³³⁻³⁵ The new product labeling also encourages "daily observation" by family members and caregivers, and it advises close communication with the prescriber if significant changes are observed.³ However, the new labeling does not endorse telephone contacts or caregiver observation as substitutes for face-to-face visits. In this study, our analysis focused on face-to-face monitoring by healthcare providers, because that is the primary clinical and quantitative focus of the new labeling. Measuring telephone contacts or caregiver monitoring would require different methodologies, because these forms of monitoring are not generally captured in claims data.

It is clear from the results of this study that improvements are needed in the timing and frequency of follow-up care for patients who start antidepressant therapy. However, it is difficult to define what level of follow-up care is a cost-effective and clinically appropriate target for healthcare providers.^{11,36} Increasing the average visit frequency for acute-care patients will increase costs for office and outpatient visits. For the patients in this study, visit costs would rise by approximately 56% if the average visit frequency increased from 4.45 to 7 visits, as recommended in product labeling. If increased visit frequency translates into improved recovery rates, the increased costs of follow-up care may be offset by reductions in other direct costs (eg, hospitalization) or by reductions in indirect costs (eg, absenteeism). In the absence of solid research data, these linkages remain speculative.

Given the costs associated with more frequent office visits, it will be important to determine the conditions for which increased visit frequency is clinically appropriate. As a precautionary measure, the FDA recommends close monitoring for *all* new episodes of antidepressant use, but the clinical support for close monitoring varies by indication and age group. The data are strongest for children and adolescents who use antidepressants for major depressive disorder, for whom the risk of suicidality is likely to be highest. However, the risk in this age group may extend to anxiety disorders, which also are frequently treated using antidepressants. The new black box warning was based on the results of a pooled analysis that included pediatric trials for both anxiety disorders and depressive disorders, although the pattern of suicidality risk was not as consistent for OCD as for major depression.^{2,5,6}

For adult users of antidepressants, most attention has been focused on the possible increase in suicidality in patients with major depressive disorder.^{3,9} However, the FDA's current review of this risk includes an analysis of all studied indications in adult patients, paralleling its analysis of the pediatric trials.⁹

The results of the FDA review will help determine whether close monitoring for suicidality is clinically appropriate for adult patients who begin using antidepressants for conditions other than major depression. In the current study, our measures of visit frequency were pooled across all treated conditions. These measures are consistent with the new product labels, which set the same monitoring targets for all indications. However, the new targets may be overly aggressive for some clinical applications of antidepressants, such as autism in children or smoking cessation in adults. As a result, our analysis may overestimate the gap between usual care and what may be viewed as more appropri-

ate—and more cost-effective—clinical practice for some patients.

This study assesses clinical practice during the years just before the widespread introduction of suicidality warnings in antidepressant product labeling. The results provide a baseline for future research to evaluate whether follow-up care has improved since the new labeling was introduced. The study also provides a baseline for assessing whether the incidence of antidepressant treatment has declined in response to the new warning language. Concerns have been raised in the professional community that the strong black box warnings may inappropriately reduce access to antidepressant drugs in populations that could benefit from them.^{26,37}

In this study, incidence rates for antidepressant treatment showed some striking differences by age and sex. Adult women were more likely than adult men to be treated with antidepressants, but the relative incidence by sex was reversed for children age 12 years and younger. The higher rate of antidepressant use by women has been frequently reported, and it is consistent with the higher incidence of depressive disorders in women.³⁸ However, the higher incidence of antidepressant use by young boys (aged 12 years and younger) has not been as widely noted, and it does not appear to be associated with the treatment of depression. For young boys, the conditions most commonly treated with antidepressants are OCD, autism, and anxiety.³⁹ Boys are substantially more likely than girls in this age group to receive antidepressants for these 3 conditions.³⁹ In the current study, younger children generally had lower frequencies of office visits than adolescents after they began using antidepressant medications. For the conditions that predominate in younger children (anxiety disorders and autism), less frequent office-based monitoring appears to be the norm.

Limitations of the Study

The findings of this study are based on treatment patterns in a large, commercially insured population and may not generalize to other populations. The visit rates observed here are not likely to generalize to Medicare or uninsured patients, because visit rates tend to be significantly lower in these populations.^{21,40} As a result, this study probably underestimates the level of the treatment gap in the general population.

The use of medical claims to identify follow-up visits for antidepressant medication management can be problematic. Some visits for mental health treatment may not be coded as such, and some ambulatory visits scheduled for other purposes may include evaluation of the patient's response to antidepressant therapy. To

address this limitation, the study measured visit rates using a range defined by mental health visits at the lower bound and all ambulatory visits at the upper bound. Measuring only the visits that are coded for mental health is likely to underestimate the actual rate of follow-up visits, and measuring all ambulatory visits is likely to overestimate the number of visits that addressed patients' use of antidepressants. Because significant gaps in care were observed even when all ambulatory visits were included, it is likely that this study underestimates the treatment gaps in usual practice.

Another limitation of medical claims is that the diagnosis associated with a patient's use of antidepressants may not be recorded in the billing data for office visits. This makes it difficult to evaluate whether visit frequencies vary by treated condition, and whether this variation is consistent with clinical best practice. The appropriate level of follow-up monitoring is likely to vary by age group and indication, although the evidence to guide practice variations still is limited. A fruitful subject for future research is to measure and evaluate visit frequencies in the context of more detailed diagnostic data for adult and pediatric patients.

CONCLUSION

When adults and children begin a new course of antidepressant therapy for any indication, they tend to receive far less follow-up care than is recommended by the current product labeling. These treatment gaps create a dilemma for the healthcare system. Although better follow-up care is clearly desirable, increasing the frequency of outpatient and office visits will increase the costs of care. No research evidence is currently available to help clinicians determine what level of follow-up care is most cost-effective. One challenge for future research is to identify patterns of follow-up care that are most likely to improve health outcomes, while minimizing costs and the risk of adverse events. As with any treatment for which there is evidence of benefit as well as potential harm, early and frequent follow-up after the initiation of antidepressant therapy is the prudent course until more definitive research becomes available.

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