Costs of Antidepressant Medications Associated With Inadequate Treatment

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Objective: To determine the costs of antidepressant medications used during inadequate treatment.

Study Design: Retrospective database analysis of pharmacy claims made by patients who were treated under routine clinical conditions from July 1, 1999, through September 30, 2002.

Patients and Methods: Our participants included 21 632 patients enrolled in a commercial HMO who had a primary care physician associated with our healthcare system. Patients never receiving at least a minimum likely effective antidepressant dose for at least 90 days were defined as having inadequate treatment. This study calculated the costs of antidepressants involved with inadequate treatment at the level of the patient and the medication trial.

Results: A majority of patients (51%) received inadequate treatment. Of overall antidepressant costs, 16% were incurred during trials for patients never adequately treated. The majority of inadequate trials were short and unlikely to have been effective. Most patients (64%) had only a single trial of antidepressants. Venlafaxine, fluoxetine, and sertraline had significantly lower first-trial inadequacy rates compared with the most commonly prescribed agent, citalopram.

Conclusions: Improved patient care quality and lower antidepressant costs could result if clinicians and healthcare systems focus on reducing short trial rates. Initiating treatment with agents least likely to be discontinued prematurely may be helpful.

(Am J Manag Care. 2004;10:357-365)

Antidepressants are among the most frequently prescribed medications in the United States, accounting for approximately 14% of the total US outpatient pharmacy costs in 2000.[1] Antidepressant use rates and costs are projected to increase throughout the coming decade,[1] driven in large part by the increasing recognition and treatment of both mood and anxiety disorders by physicians in general medical settings.[2] Despite the high frequency of antidepressant use, concerns have been raised regarding the effectiveness of current prescribing practices.[3-6]

The goals of antidepressant treatment for mood disorders are full remission of symptoms and prevention of relapse. Doses need to be sufficient to produce symptom resolution, and treatment needs to continue for a sufficient duration (4-12 months beyond symptom resolution) to reduce the likelihood of relapse.[7-13] Courses of treatment failing to meet these targets are likely to be suboptimal and can be regarded as inadequate treatment trials.[4,10,14-16]

Treatment goals for the use of antidepressants in patients with anxiety disorders are very similar, and guidelines for anxiety disorders have minimum dose and duration targets[5,17-21] nearly identical to those in mood disorder guidelines. Mood and anxiety symptoms frequently appear together in patients in general medical settings,[22-25] and primary care physicians (PCPs) base decisions to use antidepressants more on symptom severity than on diagnosis.[26,27] Because underdiagnosis and undertreatment of mood and anxiety disorders are common,[3] and rates of false-positive diagnosis by PCPs of mood, anxiety, and other mental disorders are relatively low,[26] provision of antidepressant medication for patients without an appropriate indication is unusual.[28] These factors argue in favor of including a broad spectrum of patients receiving antidepressants when undertaking an assessment of antidepressant treatment.

Rates of inadequate antidepressant treatment are high in part because many patients discontinue treatment early.[6,13,14,29-32] Little attention has been devoted to the costs incurred by healthcare systems and HMOs in payment of pharmacy claims made by covered patients who use antidepressants for short, inadequate courses of treatment.[33,34] We hypothesized that a large fraction of the total acquisition cost of antidepressants was associated with treatment considered inadequate

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This study was supported in part by a grant from Wyeth Pharmaceuticals (who played no role in the collection, analysis, interpretation of, or decision to publish the data) and by the Massachusetts General Hospital's Primary Care Operations Improvement and Clinical Research Programs.

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due to premature discontinuation. To evaluate this hypothesis, we conducted a retrospective analysis of antidepressant use patterns and their associated acquisition costs for patients prescribed antidepressants in a large HMO.

METHODS

Data Source

We analyzed pharmacy records from an HMO from July 1, 1999, through September 30, 2002. Patients in this dataset had a PCP in the Partners HealthCare System, a network of academic and community PCPs and specialists in Eastern Massachusetts.

No formulary restrictions, mental health carve-out, or depression management program impacted the study population during the time the data were collected. There was a 3-tier drug copayment program. This program varied by employer; but in general, during 2002, most patients paid $5-$10 per month for generic antidepressants, which were in the lowest tier; $20 for most other antidepressants; and $35 for weekly brand-name fluoxetine, the only antidepressant in the top tier.

Prescription records showing the fill date, drug name, dose, number of pills supplied, and name of prescriber from retail and mail order pharmacies were collected. After correction of data entry errors, 2.61 million prescription records for 161 132 patients with costs totaling $95.6 million were available for analysis.

A total of 26 414 patients (16.4% of the patients in the database) received 230 924 antidepressant prescriptions (8.9 % of total prescriptions). These antidepressant prescriptions totaled $16.0 million (17.0% of total pharmacy costs for all medications). Copayment costs incurred by patients were unavailable; hence, they were not included in this analysis.

Table 1. Minimum Average Daily Doses, Low-Dose Thresholds, and Most Common Doses*

Drug Name	Minimum Average Daily Dose Required for Adequacy (mg)	Threshold for Low-Dose Trials	Most Commonly Prescribed Daily Dose (mg)
Escitalopram	10	N/A	10
Mirtazapine and phenelzine	15	N/A	30
Citalopram, fluoxetine, and paroxetine	20	N/A	20
Paroxetine CR	25	N/A	25
Tranylcypromine	30	N/A	90
Isocarboxazid	30	N/A	40
Sertraline	50	N/A	50
Venlafaxine	75	N/A	150
Nortriptyline	75	25 mg/day	50
Amitriptyline	125	50 mg/day	100
Doxepin	125	50 mg/day	75
Clomipramine	125	25 mg/day	150
Trimipramine	125	25 mg/day	100
Desipramine and imipramine	125	25 mg/day	50
Protriptyline	125	25 mg/day	20
Bupropion	150	N/A	300
Fluvoxamine	150	N/A	100
Maprotiline	225	25 mg/day	225
Amoxapine	250	25 mg/day	75
Nefazodone	300	N/A	300
Trazodone	300	100 mg/day	150

*N/A indicates not applicable.

Exclusions

An individual treatment trial was defined as 1 or more continuous prescriptions of the same antidepressant. If a gap of more than 120 days between prescriptions occurred, a new trial was considered to have begun unless the prescription written before the gap provided sufficient days of medication therapy to bridge the gap period.

Tricyclic antidepressants (TCAs) and trazodone in low doses are commonly used for treatment of chronic pain, insomnia, and other conditions for which mood disorder guideline concordance is not relevant. We eliminated the 5584 trials involving only

low-dose TCAs or trazodone, excluding 2572 (9.7%) patients. The excluded trials represented only $47 200 or 0.3% of all of the antidepressant pharmacy costs. **Table 1** lists the low-dose thresholds.

Data on enrollment duration were available for most members (99.1%) in the database. When we did not have enrollment data, we used pharmacy fill dates as proxies for enrollment periods. Patients without evidence of more than 180 days of membership in the plan were eliminated from the analysis.

Final Analytic Sample

After excluding low-dose TCA and trazodone trials and patients with short enrollment periods, 21 632 patients remained for analysis. A total of 203 081 antidepressant pharmacy records remained; the corresponding total cost of the medication was $15.6 million.

Definition of Treatment Inadequacy

Treatments that failed to achieve use of minimum likely effective doses and/or were prematurely discontinued were defined as inadequate. The minimum likely effective dose for each agent (Table 1) was derived from literature review and practice guidelines.[12,35] To make comparisons between agents, all antidepressants were first adjusted to a "fluoxetine equivalence" based on equating their minimum daily dose as displayed in Table 1 to 20 mg of fluoxetine. We then examined patterns of use. The distribution of actual mean daily dose based on an expected use of 20-mg fluoxetine equivalents per day showed a close clustering between 18.75 and 20 mg/day. A mean daily dose of approximately 18.75 mg is achieved if patients miss 2 daily doses in a 30-day period. We set the minimum threshold for dose adequacy at 18.75 mg of fluoxetine equivalents per day, as this allowed patients with less-than-perfect adherence still to be considered as receiving an adequate dose, while also reflecting the gap between this pattern of use and the cluster reflecting use of lower doses.

We examined every period within a trial, beginning and ending with a prescription fill date, and calculated the average daily dose and the cumulative length of the trial for each of these periods, looking for at least 1 90-day period during which our minimum daily average dose was achieved. Thus, patients could have a period of dose titration at the beginning of a trial and still achieve adequacy by having at least 90 days in the middle of the trial during which they received an adequate dose. The last prescription in a trial was used only to indicate the date by which the medication in the previous prescription had been consumed. Pills dispensed in the final prescription were not included in our calculations because we could neither assume that all of these pills were consumed, nor know the time period it took for their consumption. Patients with more than 1 treatment trial were considered to have had adequate treatment if any 1 of their trials met adequacy criteria.

Patients were divided into 2 groups: those who received at least 1 period of adequate treatment and those who never received adequate treatment. All of the trials for patients who never received adequate treatment are grouped into "all trials for inadequately treated patients" (**Table 2**). In contrast, "all trials for adequately treated patients" included some inadequate trials. This is because patients with adequate treatment may have had some trials that were inadequate. For example, a patient may have had a short trial, been switched to another agent, and had an adequate trial of the second agent. Within these 2 groups of patients, we stratified trials by trial duration.

Definition of Provider Type

Every pharmacy record specified the prescribing physician and patient's PCP. Prescribers were assigned to 1 of 3 categories: PCPs, psychiatric specialists, or "other." Others were nonpsychiatric specialists, hospital residents, unknown doctors, and those records with invalid and/or unidentified Drug Enforcement Administration numbers. Within the "other" category, the largest group was nonpsychiatric specialists (50.0%).

Analytic Methods

"No refill trials" involved only a single prescription. More than 82% of these single prescription trials were for fewer than 90 pills, and 50% of these prescriptions were for 30 pills or fewer. Trials between 0 and 90 days were defined as having at least 1 refill but no refills beyond a 90-day cutoff. Trials in this group were sufficiently below duration guidelines for mood and anxiety disorders that it was unlikely that treatment during these trials was effective.

Trials of at least 90 days but fewer than 180 days were considered adequate if the minimum dose threshold was reached for at least 90 days. Although these trials were shorter than suggested by most guidelines, there was at least a reasonable chance, across a population, that some benefit would have been achieved. Trials of more than 180 days were generally considered guideline concordant for mood and anxiety disorders if they included sufficient sustained doses. By further subdividing these longer trials, we also were able to assess the costs and frequency of those trials extending beyond typical recommendations, a target of some cost-control strategies.

Each pharmacy record included a cost variable indicating the amount the HMO reimbursed the pharmacy.

Table 2. Cost of Adequate and Inadequate Treatment Stratified by Trial Length

Trial Length in Days	Trials		Cost of Trials (× 1000)	Percentage of Total Cost	Cost per Trial
	No.	Percent			
All Trials for Adequately Treated Patients*					
No refills	2720	7.9%	$202	1.3%	$74
0-90	2002	5.8%	$348	2.2%	$174
91-180	4004	11.8%	$1495	9.6%	$370
181-360	4813	14.0%	$3117	19.9%	$648
361-540	2297	6.7%	$2427	15.5%	$1057
>540	2917	8.5%	$5690	36.4%	$951
Total	18 753	54.7%	$13 279	84.9%	$707
All Trials for Inadequately Treated Patients					
No refills	7327	21.4%	$491	3.1%	$67
0-90	4344	12.7%	$676	4.3%	$156
91-180	1816	5.3%	$342	2.2%	$188
181-360	1253	3.7%	$391	2.5%	$312
361-540	367	1.1%	$180	1.2%	$491
>540	385	1.1%	$283	1.8%	$735
Total	15 492	45.3%	$2363	15.1%	$153

*Including inadequate trials before and/or after their adequate trial(s).

This was the sum of the price paid by health plan for the drug plus a small administrative reimbursement (usually $0.28), minus the cost of the copayment made by the plan member. We used this cost variable for all cost calculations in this paper. For each trial, the cost of each prescription filled during the trial was summed to provide the total cost of the trial. In evaluating adequacy rates for individual antidepressant products, we limited our analysis to the first trial for each patient.

We used SAS software version 8.0 for all analyses (SAS Institute Inc, Cary, NC). We performed descriptive comparisons of adequacy rates by antidepressant type, with adequacy rates calculated as the ratio of the number of patients with adequate trials to the total number of patients with trials. Multivariate logistic regression models were used to assess statistically significant predictors of inadequate antidepressant treatment, including physician specialty, patient age and sex, and specific antidepressant drug. In regression models, we evaluated a variety of small incremental changes in dose and duration, and noted no significant change in our findings. Doubling and tripling the minimum likely effective dose produced a significant change in adequacy outcomes, and these results for several of the most common drugs are displayed in the **Figure.** We calculated adjusted odds ratios and 95% confidence intervals, and considered a 2-tailed *P* value of <.05 to be statistically significant.

RESULTS

We evaluated patients treated with antidepressants. These patients received 34 281 distinct antidepressant trials. On a patient level of analysis, 51% received inadequate treatment. These patients received 45.2% of all trials (Table 2). Costs of these trials to the heath plan were $2.4 million, representing 15% of the total $15.6 million spent on antidepressants.

Categorized by trial length, the largest group of trials were single-prescription trials for inadequately treated patients (21.4%). As expected, longer trials, on average, cost more than shorter trials. Trials of the same length cost more if they were for adequately treated patients (Table 2).

In this study, the number of patients who had only a single trial was 13 863 (64%). The remaining 7769 (36%) patients received multiple trials: 4859 (22%) received 2 trials, 1755 (8%) received 3 trials, and 1155 (5%) received more than 3 trials.

In order to provide a fair comparison between agents, only the first trial each patient received was included in the analysis to determine rates of adequacy of individual drugs (**Table 3**). Among drugs with more than 250 trials, those with the lowest rates of inadequacy were venlafaxine, fluoxetine, sertraline, citalopram, and mirtazapine. Compared with citalopram (the most fre-

quently prescribed drug in the Partners system), venlafaxine, fluoxetine, and sertraline all had first-trial rates of inadequacy significantly lower than that of citalopram. Drugs with the highest rates of first-trial inadequacy were trazodone, amitriptyline, and bupropion. Nefazodone, paroxetine, and nortriptyline had rates of adequacy similar to that of citalopram.

In multivariate regression analyses accounting for confounding factors (including age, sex, antidepressant prescribed, and prescriber type), younger age but not sex was a significant predictor of treatment inadequacy (**Table 4**). The strongest predictors of inadequate treatment were use of amitriptyline or trazodone. Trials for patients under the age of 20 years also were likely to be inadequate. Predictors of adequacy included use of fluoxetine, sertraline, or venlafaxine. Those trials prescribed by more than 1 prescriber type were less likely to be inadequate than those prescribed by a single prescriber type. Trials with prescriptions written by PCPs or other specialists alone were more likely to be inadequate than those with psychiatrists prescribing alone.

To determine whether prior antidepressant use impacted the likelihood of adequacy for subsequent tri-

Figure. Rate of Adequacy: First Trials Only

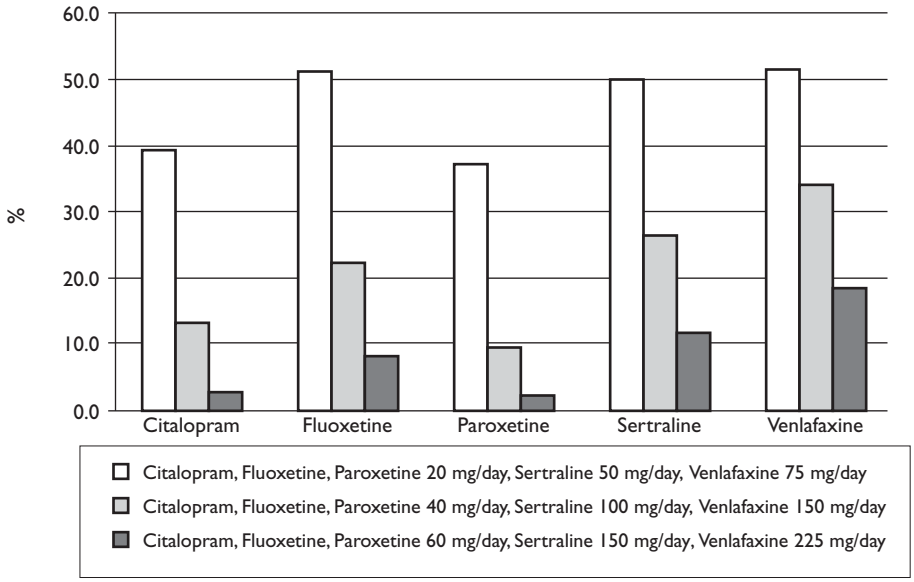

Table 3. Rates of Adequacy and Costs by Antidepressant Agent: First Trials Only

Drug Name	Adequate Trials		Inadequate Trials		Total Trials		
	No. of Trials	Cost (×1000)	No. of Trials	Cost (×1000)	No. of Trials	Cost (×1000)	Rate of Adequacy
Amitriptyline	53	$5	269	$9	322	$14	16.5%
Bupropion	1123	$1030	2297	$261	3420	$1291	32.8%
Citalopram	1689	$1116	2604	$326	4293	$1442	39.3%
Fluoxetine	1813	$2864	1748	$446	3561	$3310	50.9%
Mirtazapine	91	$89	139	$19	230	$108	39.6%
Nefazodone	147	$164	291	$68	438	$232	33.6%
Nortriptyline	102	$30	209	$11	311	$41	32.8%
Paroxetine	1211	$1119	2047	$422	3258	$1541	37.2%
Sertraline	1936	$1675	1947	$280	3883	$1955	49.9%
Trazodone	18	$6	264	$15	282	$21	6.4%
Venlafaxine	510	$686	485	$90	995	$776	51.3%
Others	202	$264	437	$98	295	$362	35.3%
Total	8895	$9048	12 737	$2045	21 288	$11 093	41.1%

Table 4. Multivariate Predictors of Inadequate Antidepressant Treatment: First Trials Only*

Drug Name or Prescriber Type	No. of Trials	Adjusted Odds Ratio†	95% Confidence Interval
Amitriptyline	322	2.44	(1.88, 3.18)
Bupropion	3420	1.22	(1.11, 1.34)
Citalopram	4293	1.00	—
Fluoxetine	3561	0.70	(0.64, 0.77)
Mirtazapine	230	0.97	(0.73, 1.28)
Nefazodone	438	1.25	(1.01, 1.53)
Nortriptyline	311	1.21	(0.95, 1.56)
Paroxetine	3258	1.08	(0.98, 1.19)
Sertraline	3883	0.65	(0.59, 0.71)
Trazodone	282	2.15	(1.65, 2.80)
Venlafaxine	995	0.67	(0.58, 0.77)
Others	22	1.33	(1.11, 1.59)
Primary care physician only	9057	1.00	—
Psychiatrist only	6304	0.44	(0.41, 0.47)
Other only	3341	1.19	(1.10, 1.30)
Any 2 prescriber types	2708	0.20	(0.18, 0.22)
Primary care physician, psychiatrist, and other	222	0.10	(0.07, 0.14)

*Test statistics such as the likelihood ratio (486, $df = 11$; $P >$ chi-square $< .0001$) and the Wald test statistic (476, $df = 11$; $P >$ chi-square $< .0001$) confirm that our model fits reasonably well.
†Adjusted odds ratio of the likelihood of inadequate antidepressant treatment, simultaneously adjusted for all variables. Age and sex were variables in the analysis.

als, we examined the 3787 patients (17% of the 21 632 patients originally analyzed) who began a trial after the midpoint of the observation period and who had been represented in the dataset for the entire period. This revealed that prior antidepressant use made a trial significantly less likely to be inadequate compared with no prior antidepressant use. Limits in our sample size did not allow us to consider the potential impact of prior trials as a factor in the comparison of inadequacy among agents.

We considered how many additional patients would have had an adequate trial if we included the final prescription in the analysis. If all pills in the final prescription of multiprescription trials were consumed at a rate of 1 pill per day, an additional 1315 patients (6%) would have received adequate treatment, and the overall rate of adequacy would have increased from 49% to 55%. However, this is very likely to overstate the impact of including final prescriptions because not all tablets are likely to be consumed, and even if they are, they may not be consumed quickly enough so that the mean dose per day remains adequate.

We conducted an additional analysis to determine the impact of removing TCAs and trazodone, because it is possible that these agents may be used for purposes other than treating anxiety or depression. This removed only 859 patients (4%) and resulted in only a modest increase in treatment adequacy, from 49.0% to 49.8%. The percentage of antidepressant costs for patients never treated adequately remained at 15%.

COMMENT

This retrospective analysis of antidepressant use in routine clinical conditions found that inadequate treatment is very common, and that a substantial portion of antidepressant acquisition costs are spent in ways unlikely to produce desired outcomes.

A majority (51%) of patients had only inadequate treatment. That is, at no time during the 39 months of observation did they simultaneously receive treatment that achieved dose and duration minimums. Resources expended on medications used by these patients represent 15% of total antidepressant costs. Given the evidence suggesting that, on a population basis, treatment failing to attain minimal guideline standards is unlikely to produce optimal outcomes,[10,14,15,36,37] these resources may be regarded as having been expended suboptimally.

Spending for inadequate treatment was almost certainly suboptimal in cases where patients had only 1 prescription and this prescription was never refilled. It is unlikely that patients receiving very short (0-30 days of duration) trials achieve sustained medication-induced symptom remission, and protection against relapse is low.[7,37-39] Single prescriptions (where no subsequent refills or prescriptions for a different antide-

pressant appeared) accounted for 21% of all trials, and 3% of total costs.

Various strategies, such as PCPs instructing patients about the importance of continuation[7] or the use of care managers,[37,39] may reduce rates of inadequate treatment. Our findings suggest that strategies focused on reducing the likelihood of short trials also may reduce rates of inadequate treatment. Such strategies would impact a large number of patients. They may reduce the medication acquisition costs associated with inadequate treatment, and thereby reduce suboptimal, potentially wasted expenditures. These strategies would support both quality improvement and cost-control goals, and should be considered by healthcare systems.

One way to reduce the prevalence of short trials may be to increase the use of agents with lower inadequacy rates (ie, those least likely to be prematurely discontinued). Comparing inadequacy rates across agents may be helpful in identifying these agents. We found that venlafaxine, sertraline, and fluoxetine were significantly less likely than other commonly used agents to be discontinued prematurely.

Several limitations must be considered before our findings can be used to guide the choice of antidepressant agent. We were not able to determine why venlafaxine, sertraline, and fluoxetine had lower inadequacy rates than the commonly used reference agent, citalopram, or the less commonly prescribed agents. Our comparison among agents was based only on first trials and required only that patients use minimum likely effective doses. Treatment episodes meeting minimum dosage and duration thresholds do not necessarily produce optimal outcomes, and lower inadequacy rates do not guarantee the best outcomes. Truly optimizing outcomes may frequently require doses beyond these minimal levels. In our analysis, several drugs, including venlafaxine, were most likely to be used at doses above the minimum. This may suggest that a larger fraction of patients treated with these drugs may require doses higher than the doses used in our analysis. Although each agent's minimum likely effective dose was based on expert consensus and manufacturers' guidelines, efficacy and effectiveness data supporting these thresholds are limited.

Healthcare organizations seeking to control costs may encourage the use of antidepressants with the lowest acquisition costs. Many currently use this strategy, but its value remains unproven. If inexpensive agents such as TCAs have high inadequacy rates, choosing these agents may reduce quality. Total costs of care (as opposed to costs of purchasing medications) may not increase when agents less likely to be prematurely discontinued (eg, agents with low inadequacy rates) are used, even if such agents are relatively expensive.[40-42] Consideration of relative inadequacy (and eventually adequacy) rates for various medications may assist healthcare organizations in making informed choices of preferred agents.

The 49% of patients who received adequate treatment accounted for 55% of trials and 85% of antidepressant acquisition costs. Some of the patients in this group (44%) had multiple trials. Among these were trials that were inadequate (18% of total trials). These typically were short trials for patients who went on to adequate treatment, often after being switched to a different medication. These trials made up only a small fraction (6%) of antidepressant costs. In contrast to spending for patients who never had adequate treatment, money spent on short trials for patients with switches and adequate treatment may not represent suboptimal use of resources. This is because some amount of switching may be inevitable, and may be appropriate, so long as the patient eventually receives adequate treatment with desired outcomes.[7,9] It may not be reasonable to focus on trying to reduce this segment of antidepressant spending.

Twenty-one percent of adequate trials were of long duration (>540 days). These trials accounted for 36% of the total antidepressant acquisition costs. Discontinuation of long trials may have a negative impact on outcomes unless executed with care. Patients with multiple episodes of mood disorder, or whose mood or anxiety symptoms reappear and persist when antidepressants are discontinued after adequate periods of treatment, may require long-term treatment.[43] It may be difficult in routine clinical settings to discriminate between patients who should and should not continue long term.

Previous studies found rates of treatment adequacy similar to those reported here. Some of these studies included only patients with depression,[7,44,45] while others included patients treated with antidepressants for a variety of disorders.[46] Variation in adequacy as a function of the particular antidepressant drug provided[30] and the impact of adequacy on costs[41] have been noted, but methodological differences complicate comparison of those results with ours. When overall clinical outcomes are considered, factors other than antidepressant treatment adequacy (eg, use of psychotherapy, frequency of return visits) are known to be important.[10,47] The relevance of adequacy for patients with mild depression has been questioned.[45] There is general agreement, however, that reducing rates of short trials and use of sufficient dosing will improve rates of remission, lower rates of relapse, and reduce illness burden.[8]

Among other limitations of this work is that patients receiving antidepressants did not have confirmation of diagnosis by standard rating techniques. Some unknown fraction of patients may have been prescribed antidepressants for pain, insomnia, or other conditions where guideline concordance is not relevant. This fraction, however, is likely to have been small. Several studies suggest that false-positive diagnosis of mood and anxiety disorders is rare,[26] and that a substantial majority of patients prescribed antidepressants in routine general medical settings have a mood or anxiety problem for which guideline-concordant treatment is indicated.[2] Removing trazodone and TCAs, which may have been more likely to have been prescribed for insomnia or pain, from the analysis did not have a significant impact on the findings. However, our conclusions must be regarded as preliminary until studies linking diagnosis and adequacy are completed.

Another limitation of this work is that because clinical outcomes were not directly measured, the relationship between failure to achieve minimal guideline standards and poor outcomes was inferred based on other studies.[10,14,15,36,37] This relationship is strong enough to form the basis of widely accepted treatment guidelines, but is by no means definitive.

Other study limitations were that we did not measure costs to patients (copayments), nonpharmacy costs (eg, cost of medical care), or indirect costs (eg, costs of disability). These costs are larger than the pharmacy costs measured here. The use of free drug samples was not measured, but would have produced lower inadequacy rates, particularly for newer agents. Nondrug factors, such as patient and physician demographics, belief systems, level of comorbidities, and severity of primary illness, were not taken into account. The studied population included only employed, commercially insured individuals residing in urban and suburban Eastern Massachusetts communities, whose medication use patterns may not necessarily be nationally representative. These factors should be included in follow-up studies, so that a complete picture of antidepressant use can be obtained. Despite its limits, this approach makes it possible to include the large fraction of patients typically excluded from prospective studies[48] and provided an assessment of patterns of antidepressant use under "real world" conditions.

In conclusion, these findings indicate that the majority of patients prescribed antidepressants under routine clinical conditions had inadequate treatment—treatment that never met minimum guideline standards. In most cases, treatment was inadequate because it was terminated prematurely (the duration was very short). Achieving and sustaining desired antidepressant treatment outcomes involve complex factors, and treatment adequacy may be a necessary, although not sufficient, component of this process. Healthcare systems might take a first step toward improving adequacy by focusing on reducing short trials. This may involve increased attention to patient education and the initiation of treatment with agents most likely to result in adequate trials. Improving adequacy by reducing short trials may be an appropriate way to control antidepressant costs and may improve the quality of care for a large portion of the patient population.

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