

Cost-effectiveness of Treatments for Major Depression in Primary Care Practice

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Background: This study augments a randomized controlled trial to analyze the cost-effectiveness of 2 standardized treatments for major depression relative to each other and to the “usual care” provided by primary care physicians.

Methods: A randomized controlled trial was conducted in which primary care patients meeting DSM-III-R criteria for current major depression were assigned to pharmacotherapy (where nortriptyline hydrochloride was given) or interpersonal psychotherapy provided in a standardized framework or a primary physician’s usual care. Two outcome measures, depression-free days and quality-adjusted days, were developed using information on depressive symptoms over time. The costs of care were calculated. Cost-effectiveness ratios comparing the incremental outcomes with the incremental costs for the different treatments were estimated. Sensitivity analyses were performed.

Results: In terms of both economic costs and quality-of-life outcomes, patients assigned to the pharmacotherapy group did slightly better than those assigned to interpersonal psychotherapy. Both standardized therapies provided better outcomes than primary physician’s usual care, but each consumed more resources. No meaningful cost-offsets were found. The incremental direct cost per additional depression-free day for pharmacotherapy relative to usual care ranges from \$12.66 to \$16.87 which translates to direct cost per quality-adjusted year gained from \$11 270 to \$19 510.

Conclusions: Standardized treatments for depression lead to better outcomes than usual care but also lead to higher costs. However, the estimates of the cost per quality-of-life year gained for standardized pharmacotherapy are comparable with those found for other treatments provided in routine practice.

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THE RELIANCE on market forces to allocate health care resources has placed more emphasis on understanding the efficiency of health care delivery. At the same time, concerns with quality and health plan accountability have heightened interest in assuring that effective clinical treatments are being used for treatment. Some of the organizations that develop report cards use the treatment of major depression as one of the markers for the quality of care provided within health plans.¹⁻³ Cost-effectiveness provides useful information for programmatic and policy decisions that must balance costs and outcomes of care. This study augments a randomized controlled trial of treatments for major depression within primary care to analyze the cost-effectiveness of 3 clinical strategies.

Our approach builds on recommendations of the Panel on Cost-Effective-

ness in Health and Medicine for conducting such research.⁴ The innovations in our current article include use of a randomized trial within primary care settings, a careful accounting of treatment-related resource use, the transformation of information from symptom scales into quality-adjusted life years for purposes of comparison with other medical technologies, and a rigorous statistical evaluation of cost-effectiveness ratios. The treatment strategies studied are consistent with the Agency for Health Care Policy and Research guidelines for treatment of depression in primary care.⁵ The interventions studied involve interpersonal psychotherapy (IPT), pharmacotherapy using a tricyclic antidepressant, nortriptyline hydrochloride (NT), that continues to account for a substantial portion of all treatment for major depression (about 25%), and primary physician’s usual care (UC).

MATERIALS AND METHODS

THE TREATMENTS

This study uses information from a clinical trial conducted by Schulberg et al^{6,7} that has been fully described elsewhere. Primary care patients were randomized to 1 of 3 treatment arms: NT, IPT, or UC. Patients randomized to NT were treated by either board-certified family practitioners or general internists trained in standardized NT procedures. The NT protocol consisted of weekly or biweekly acute-phase visits until the patient's blood level reached a consistent therapeutic state (190-270 nmol/L) and depressive symptoms had improved. A continuation phase was then initiated and patients were seen monthly for 6 months. Patients randomized to IPT were treated by psychiatrists and clinical psychologists trained in its standardized application which consisted of approximately 16 weekly acute-phase sessions followed by 4 monthly continuation-phase sessions. Both standardized treatments were provided free of charge to patients. In the study's UC arm, the investigators informed both the primary care physician and patient that the patient was experiencing a major depression. Usual care consisted of whatever strategy the primary care physician and patient chose to follow.⁸

BACKGROUND AND OUTCOME MEASURES

The patients' psychiatric and physical health status and sociodemographic characteristics as measured at baseline are presented in **Table 1**. Our goals in constructing health outcome measures were to (1) develop summary measures using information on symptoms over time and (2) create a utility-based indicator of outcome. The Hamilton Rating Scale-Depression⁹ (HRS-D) and the Beck Depression Inventory¹⁰ (BDI), which are highly correlated,¹¹ both measure depressive symptoms and generate values indicating whether individuals are considered symptom free (≤ 7 on the HRS-D and ≤ 8 on the BDI) or severely depressed (≥ 22 on both scales).¹² The HRS-D and the BDI were administered at months 1, 2, 3, 4, 6, 8, and 12 by clinical evaluators, blinded to the patients' treatment assignment.

The resulting data were used to construct an outcome measure called depression-free days (DFDs). Using HRS-D assessment scores, DFDs were calculated as follows: if patients had a HRS-D of 22 or higher, they were assumed to lack a DFD; when scoring 7 or lower, they were assumed to have a full DFD; if they scored between 7 and

22, the day was weighted proportionately. To determine the number of DFDs over a year, the scores for the baseline and first-month assessment period were added, divided by 2, and then multiplied by the number of days between assessments. This was done for all other assessment periods and the sums were totaled.

To compare the cost-effectiveness of depression treatments with those for other diseases, we transformed DFDs into quality-adjusted days by using utility weights assigned to depression based on research conducted by others. The transformation assumes a nondepressed person has a utility score of 1 (healthy) while a person meeting criteria for major depression has a utility score of 0.59—the average of 6 reported utility weights for depression¹³⁻¹⁶ (also J. Pyne, T. L. Patterson, R. M. Kaplan, S. Semple, W. L. Koch, J. C. Gillan, and I. Gran, University of California, San Diego, unpublished data, 1994). Thus, study patients were assumed to gain 0.41 of a quality-adjusted day for each day they shifted from experiencing major depression to being depression free.

SERVICE UTILIZATION AND COST MEASURES

Information on patient use of protocol-related services was obtained from records maintained for the clinical trial. This included the number of therapy visits, blood draws, and milligrams of nortriptyline hydrochloride dispensed. Information regarding use of selected services (physician visits, visits to other health care providers, prescriptions for psychotropic medications, emergency department visits, and hospitalizations) within the patients' health centers was obtained from administrative records kept by those centers. Information regarding the use of outside providers was obtained through questionnaires administered to patients during the follow-up telephone calls. All visits were classified as being of a medical or mental health type depending on the providers' qualifications. However, visits to generalist physicians were classified as mental health in nature if medical records indicated that counseling was provided, a psychotropic medication was prescribed, or the patient was referred to a mental health specialist. Hospitalizations, although recorded, were infrequent and are not analyzed because of the study's limited ability to draw inferences because of the small sample size. However, there were no significant ($P = .44$) differences in the number of inpatient days across the 3 treatment groups over the 12-month period.

Two types of cost were estimated, direct and indirect. Direct costs included the costs of medical services and

RESULTS

CHARACTERISTICS OF THE STUDY POPULATION

The 3 treatment groups did not differ in the characteristics measured at baseline (Table 1). The rather high average HRS-D and BDI scores indicate that the study population includes the very patients for whom active intervention is recommended by the Agency for Health Care Policy and Research Depression Guidelines Panel.⁵ The Duke Severity of Illness Checklist²⁶ and the Medical Outcomes Study Short Form General

Health Survey scores²⁷ indicate these patients suffer significant comorbidities.

OUTCOMES

The **Figure**, which presents the mean HRS-D score for the 3 treatment groups at each assessment point, indicates that the time path for reduction of depressive symptoms varied by treatment group. Intergroup differences in depressive status were less pronounced at 12 months than at 4 and 8 months; at 12 months, the intergroup differences in depressive status were not statistically significant albeit still possibly clinically meaningful. Differences in effective-

costs incurred in administering standardized treatments. (Administrative costs were estimated since in practice they would be incurred in monitoring guidelines.) Indirect costs included transportation and time costs incurred in obtaining services. Medical services were costed using 1995 Medicare payment rates (visits of different types and laboratory costs for blood tests). Drugs were priced at the lowest average wholesale price possible using generic costs and largest volumes as reported in the *1995 Redbook*.¹⁷ (The costs of drugs for protocol patients were based on the number of milligrams of nortriptyline hydrochloride dispensed; the costs of psychotropic medication prescribed by primary care physicians were based on the dosage prescribed.) We examined the costs of all health care services rather than those for protocol services alone since it has been posited that the cost of providing good mental health services may be "offset" by a decrease in treatment costs elsewhere.^{18,19} We estimated administrative costs at \$77 per year based on information from a managed care carve out plan²⁰ industry expert (oral communication to R. F. from J. O'Brien, MBA, Technical Assistance Collaborative of Boston, in Massachusetts, June 1977).

Transportation (bus or car) was estimated to cost \$2 per trip. Three types of time costs were estimated: travel time to and from the clinic, waiting time at the clinic, and visit time. With the exception of emergency department visits, estimated travel times and waiting times were based on national data.²¹ Estimated times for protocol visits were based on time samples of the first, fourth, and eighth therapy visits. Thus, time estimates are 50 minutes for all protocol IPT visits, 45 minutes for the initial NT visit, and 16 minutes for subsequent NT visits. Other time estimates are 20 minutes for physician visits lacking a mental health component, 30 minutes for a primary care visit with a mental health component, and 45 minutes for a visit to a nonprotocol mental health provider. The full time spent at an emergency department (waiting plus treatment time) was estimated to be 2 hours 30 minutes (T. Aubel, PhD, Department of Emergency Medicine, University of Pittsburgh in Pennsylvania, oral communication, June 10, 1997). The estimated hourly cost varied with 1989 hourly wages for people with the patient's education, sex, and age.²²

DATA ANALYSES

An intent-to-treat approach to analysis was used. Random regression methods were used to impute HRS-D and the BDI scores if an interview was missed.²³ χ^2 Tests of association or analysis of variance were performed to determine

ness, therefore, are determined by the shape of the time path for recovery. Over the 12-month period, NT, IPT, and UC patients experienced 243, 234 and 185 DFDs, respectively, when assessed with the HRS-D, and 220, 187, and 148 DFDs when assessed with the BDI. The differences across the groups are statistically significant ($F_2 = 10.11$, $P < .01$ for HRS-D; $F_2 = 8.96$, $P = .01$ for BDI).

HEALTH SERVICES UTILIZATION

Table 2 presents the mean and SD for different types of health center visits. Excluding protocol visits, NT patients made the fewest health center visits while the UC

whether health outcomes, use of services, and costs varied across the 3 treatment groups. Statistical significance was set at $P = .05$.

A cost-effectiveness ratio is a measure in which the numerator is the incremental cost and the denominator is the incremental effectiveness of an intervention compared with an alternative. To calculate cost-effectiveness ratios, we first estimated regressions to determine how costs (direct and full) and outcomes (DFDs and quality-adjusted years) varied across the treatment groups controlling for covariates (sociodemographic characteristics and baseline health status). This approach provides a more precise estimate of the difference in outcomes than does a simple analysis of variance. For each cost and outcome variable, separate regressions were run for the 2 groups being compared (NT and IPT, IPT and UC, and NT and UC). (The regression results are available from J.R.L.)

The cost-effectiveness ratios were estimated using the coefficients for the treatment group indicator in the cost and outcome regressions. In computing the ratios, we incorporated the uncertainty that exists in the estimates of incremental cost and health effects by approximating the distribution of the numerator and denominator in each ratio as normally distributed with the means and SDs derived from the regressions. We then constructed 1000 random values for the numerator and denominator which results in 1000 random values for the cost-effectiveness ratio. These formed the basis for the reported cost-effectiveness ratios, their associated asymptotic SEs and P values.^{24,25}

A number of models were estimated to determine how sensitive the cost-effectiveness estimates were to key assumptions and limitations in the data. First, we determined cost-effectiveness ratios using the 2 different depression scales. Second, we decreased the utility difference between being healthy and depressed by 0.10 point—this adjustment allows both for the possibility that the impact of depression is not so severe and that because of comorbidities, alleviating depressive symptoms will not restore somebody to perfect health. Third, we assumed that IPT could be conducted equally effectively by nonpsychiatric mental health personnel and that this reduced the cost of delivering the IPT protocol by 20%. Since the information on health service use outside the health centers was not consistently available because of missing follow-up data, most of the cost-effectiveness estimates consider the cost and use of services only within the patients' own health centers. However, we calculated cost-effectiveness ratios for a subsample of patients who responded to all follow-up interviews.

patients made the most, suggesting a possible utilization offset. However, 45% of the UC visits had some mental health component. This likely resulted from UC patients being advised to see their own physicians for treatment of depression. When protocol-specific mental health visits are added to other health center visits, both IPT and NT patients used services more intensively than UC patients.

COSTS

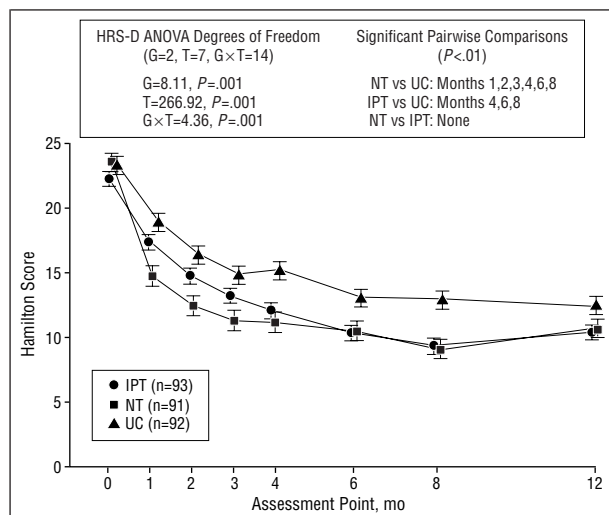
Table 3 details the costs incurred by the 3 treatment groups. It will be observed that while nonprotocol medi-

Table 1. Baseline Characteristics of Patients Randomized for Treatment of Major Depression*

Characteristic	Treatment			Statistic†	P
	Interpersonal Psychotherapy (n = 93)	Nortriptyline Hydrochloride (n = 91)	Usual Care (n = 92)		
Sociodemographic					
Mean age (SD)	37.1 (11.4)	38.6 (11.6)	38.6 (12.4)	0.63	.54
Female, %	82.8	80.2	87.0	1.52	.47
White, %	53.8	59.3	53.3	0.84	.67
Married, %	26.9	35.2	27.2	1.94	.38
Educational level of high school or higher, %	82.8	79.1	84.8	1.03	.60
Employed	42.9	44.4	40.7	0.27	.87
Mean (SD) clinical health status					
Severity of depression scores					
HRS-D	22.3 (4.6)	23.7 (5.3)	23.4 (5.3)	1.86	.16
BDI	25.0 (9.4)	25.5 (11.4)	27.3 (9.7)	1.15	.32
Physical Component Scale on the MOS	42.4 (9.6)	42.3 (9.9)	42.7 (10.9)	0.03	.97
DUSOI	34.8 (116.1)	33.3 (15.0)	34.4 (15.4)	0.22	.81

*HRS-D indicates 17-item Hamilton Rating Scale–Depression; BDI, Beck Depression Inventory; MOS, Medical Outcomes Study Short Form General Health Survey; DUSOI, Duke Severity of Illness Checklist.

†F for continuous and χ^2 for dichotomous variables.



Mean Hamilton Rating Scale–Depression (HRS-D) score for 3 treatment groups: interpersonal psychotherapy (IPT), pharmacotherapy with nortriptyline hydrochloride (NT), and primary care physician's usual care (UC). ANOVA indicates analysis of variance; G, treatment group; and T, treatment month when the reported measurement was taken.

cal care costs are higher for UC patients than for IPT and NT patients, direct costs for IPT and NT patients are significantly higher. Furthermore, the full costs incurred by IPT and NT patients significantly exceed those incurred by UC patients. It is worth noting that time and transportation costs are considerable for all groups.

COST-EFFECTIVENESS OF STANDARDIZED TREATMENTS

The data presented above indicate that NT patients do slightly better than IPT patients. The NT group's clinical outcomes as measured by DFDs are somewhat higher and costs (both direct and full) are somewhat lower although the differences are not always statistically significant in 2×2 comparisons. (In this case, a cost-effectiveness ratio is not

pertinent since such a ratio is constructed when the benefits are greater, but the costs are higher.) The comparisons between the standardized treatments and UC are more complex since IPT and NT are more expensive, but their outcomes are better. Some cost-effectiveness ratios for the standardized treatments and UC are reported in **Table 4**. Focusing on cost-effectiveness ratios NT vs UC, and using outcomes based on HRS-D scores, we found that \$13.14 in direct costs are incurred for each additional DFD experienced by NT patients. This translates into a cost of \$11 695 per quality-adjusted year if the difference between a depressed day and DFDs is 0.41 of a quality-adjusted day; and to \$15 202 per quality-adjusted year if the difference between a depressed day and a DFD is 0.41.²⁸ If full costs are considered, the cost-effectiveness ratios increase. The cost-effectiveness ratios also vary depending on the depression assessment instrument used. The cost-effectiveness ratio for IPT vs UC falls if IPT is delivered equally effectively by nonpsychiatric mental health personnel at 80% of the psychiatrist's cost per session. Using outcomes derived from HRS-D scores, the direct cost per IPT-achieved DFD would fall from \$22.82 to \$17.56; and the direct cost per quality-adjusted year 1 would fall from \$20 310 to \$15 358. It will be noted that the cost-effectiveness ratios for IPT vs UC always exceed those for NT vs UC, which is consistent with the finding that NT is slightly better than IPT in both outcomes and costs. (The findings for the subsample who responded to all follow-up interviews are similar to those presented in Table 4.)

COMMENT

In discussing the findings of their randomized clinical trial, Schulberg et al⁶ concluded that NT and IPT of a quality consistent with the Agency for Health Care Policy Research Guidelines are markedly superior to UC in resolving an episode of major depression. We used data from that trial to develop a measure called DFDs and found that NT and IPT patients achieved significantly more of

Table 2. Number of Visits Inside the Health Center for 12 Months Following Enrollment*

Visit Type	Treatment			F Statistic	P
	Interpersonal Psychotherapy (n = 93)	Nortriptyline Hydrochloride (n = 91)	Usual Care (n = 92)		
Nonprotocol visits	4.7 (4.5)	3.6 (4.8)	6.0 (5.0)	5.60	.004
Protocol visits	11.7 (8.0)	8.4 (5.7)	NA	10.53	.001
Total non-emergency department visits†	16.4 (9.9)	12.0 (7.6)	6.0 (5.0)	41.81	<.001
Emergency department visits	0.4 (0.8)	0.2 (0.6)	0.5 (1.3)	2.11	.12

*Values are expressed as mean (SD). NA indicates not applicable.
 †Indicates nonprotocol + protocol visits.

Table 3. Average Cost of Treatment by Type of Cost for 12 Months Following Enrollment*

Type of Cost, US \$	Treatment			F Statistic	P
	Interpersonal Psychotherapy (n = 93)	Nortriptyline Hydrochloride (n = 91)	Usual Care (n = 92)		
1. Nonprotocol medical costs	308.04 (353.20)	294.21 (429.92)	553.20 (490.48)	10.67	<.001
2. Protocol treatment costs	1013.53 (692.71)	920.20 (713.60)	NA	0.81†	.37†
3. Administrative costs	77.00 (0.00)	77.00 (0.00)	NA	NA	NA
4. Direct costs (1 + 2 + 3)	1398.57 (840.94)	1291.41 (842.80)	553.20 (490.48)	35.32	<.001
5. Nonprotocol service time and transportation costs	93.10 (97.25)	68.17 (90.41)	122.48 (108.17)	6.91	.001
6. Protocol service time and transportation costs	273.14 (200.43)	146.57 (107.06)	NA	28.37	<.001
7. Total time and transportation costs (5 + 6)	366.25 (242.63)	214.74 (145.95)	122.48 (108.17)	45.58	<.001
8. Costs (4 + 7)	1764.83 (1068.13)	1506.16 (974.79)	675.67 (575.29)	36.97	<.001

*Values are expressed as mean (SD). NA indicates not applicable.
 †Statistic based on comparing interpersonal psychotherapy and nortriptyline treatment only.

Table 4. Cost-effectiveness Ratios for Standardized Treatments Relative to Usual Care Using Different Indicators for Costs, Depression Outcomes, and QALYs Full Cohort*

Treatment Group/Costs, US \$	Cost per DFD				Cost per QALY 1				Cost per QALY 2			
	Outcomes Based on HRS-D		Outcomes Based on BDI		Outcomes Based on HRS-D		Outcomes Based on BDI		Outcomes Based on HRS-D		Outcomes Based on BDI	
	Mean	P	Mean	P	Mean	P	Mean	P	Mean	P	Mean	P
Nortriptyline hydrochloride vs usual care (n = 183)												
Direct costs	13.14	<.01	10.17	<.01	11 695	<.01	9051	<.01	15 202	<.01	11 766	<.01
Full costs	14.79	<.01	11.44	<.01	13 163	<.01	10 181	<.01	17 112	<.01	13 236	<.01
Interpersonal psychotherapy vs usual care (n = 185) (cost 1)												
Direct costs	22.82	.04	25.21	.74	20 310	.04	22 434	.74	26 403	.04	29 164	.74
Full costs	29.36	.04	32.44	.70	26 130	.04	28 872	.70	33 969	.04	37 533	.70
Interpersonal psychotherapy vs usual care (n = 185) (cost 2)												
Direct costs	17.56	.04	19.41	.24	15 358	.04	17 275	.74	19 965	.04	22 458	.74
Full costs	24.83	.04	26.64	.70	22 099	.04	23 710	.70	28 729	.04	30 823	.70

*DFD indicates depression-free day; QALY, quality-adjusted year; HRS-D, Hamilton Rating Scale-Depression; and BDI, Beck Depression Inventory. Direct costs are all medical costs plus administration; full costs, direct costs plus transportation and time costs. Quality-adjusted year 1 is based on the assumption that one gains 0.41 of a quality-adjusted day when one moves from being fully depressed to being symptom free; QALY 2, on the assumption that one gains 0.31 of a quality-adjusted day when one moves from being fully depressed to being symptom free; cost 1, on the assumption that interpersonal psychotherapy sessions are paid at the Medicare rate for psychiatrists; cost 2, on the assumption that interpersonal psychotherapy sessions are paid at 80% of the Medicare rate for psychiatrists.

them than UC patients. However, better mental health outcomes were achieved at a marked fiscal cost.

From an efficiency perspective, the question is whether the additional costs associated with additional

benefits are worth it. One approach to answering this question is to compare our findings against an established benchmark. Such a standard was established by a Canadian team that assigned a grade B recommendation to tech-

nologies that “were more effective than the existing ones and cost less than \$20 000 per quality-adjusted life year gained.”²⁷ The grade B recommendation was that such technologies be adopted. Using this criterion, we conclude that NT is a cost-effective alternative to UC. Interpersonal psychotherapy only meets this criterion if it can be delivered at a cost per session equal to 80% or less of the psychiatrist’s rate (which is increasingly the pattern given managed care discounting of fees and use of non-psychiatrists for psychotherapy). A second approach is to determine whether the cost-effectiveness ratios for NT and IPT relative to UC are within the ranges reported for other treatments. Since that range is very broad, both NT and IPT pass this liberal criterion.^{4,29}

It is difficult to compare our findings on cost-effectiveness for NT and IPT relative to UC with those of other researchers since, to our knowledge, this is the first study of depression treatments to apply the criteria established by the federal panel. Our general findings, however, are consistent with those of other researchers. Sturm and Wells³⁰ and Von Korff et al³¹ also found that treatment consistent with guidelines costs more money but leads to improved outcomes. Our findings also agree with those of Von Korff et al³¹ who did not find any significant medical offsets.

It is possible that our findings are biased, although it is difficult to assess the bias’ direction. On the one hand, the better outcomes found for standardized treatments may be understated relative to those that would be observed in routine practice since (1) NT patients might have been even more responsive to standardized NT if it had been provided by their regular physicians instead of by specially trained physicians; (2) physicians treating UC patients may have been more attuned to depression since they and their patients were informed of the patients’ diagnosis and knew they were being monitored; and (3) follow-up analyses ended at 12 months, but some treatment benefit could extend beyond the first year.

Alternatively, the positive outcomes for standardized treatments could be overestimated. First, nortriptyline produced physiological and psychological side-effects whose negative impact is not fully accounted for in our analyses (although any extra medical costs are). Second, our results are conditional on several key features of the experimental design. Of particular importance is that protocol treatments were provided to study subjects at no personal cost while UC subjects had to pay for mental health services within the terms of their insurance coverage. Since private insurance for mental health care typically specifies more stringent limits on coverage and requires higher levels of cost sharing, the treatment pattern for UC patients may have been adversely influenced. Thus, we could not separate the insurance effect from the protocol effect. However, a substantial number of the UC patients were covered by Medicaid where out-of-pocket effects are zero, and so the insurance effect is probably attenuated.

Since this clinical trial was undertaken, other antidepressant medications that are simpler to administer and produce fewer side effects have been marketed. However, a study conducted at Group Health Cooperative in Puget Sound³² suggests that the findings from our study

about NT would not be markedly changed by prescribing selective serotonin reuptake inhibitors. In this Group Health Cooperative study, patients recognized as depressed by their primary care physicians were randomly assigned to fluoxetine or 1 of 2 tricyclic antidepressants, and their treatment and clinical course were followed for 6 months. Although patients often switched from one medication to another, the outcomes and costs did not differ between the classes of antidepressants.

The data from this study come from a randomized clinical trial. While many have recommended using information from this source to conduct cost-effectiveness studies,³³ others question whether such results are generalizable to routine practice.³⁴ We would note, therefore, that the randomized clinical trial’s inclusionary criteria were broad, the exclusionary criteria were limited, and patients were recruited in the waiting rooms of primary care practices. Thus, our findings should generalize better to an ambulatory medical population treated in routine practice³⁵ than is common. A second influence of the clinical trial is that subject recruitment was determined by the numbers needed to assess recovery from depression. Thus, the number of cases was too small to detect any significant differences in rare events such as hospitalizations. Finally, the data from the trial were subject to attrition. While our analyses of this problem suggest that the clinical results are stable to differences in attrition, our ability to clarify this issue is limited and we must interpret the results cautiously. On balance, however, we believe that reported estimates on the cost-effectiveness of standardized treatments for depression are likely to encompass those to be found in routine practice.

The growth of managed care has changed the manner in which clinical decisions are made. They are no longer predominantly the result of interactions between individual clinicians and individual patients but, instead, are increasingly influenced by administrative and fiscal mechanisms. Expanded use of treatment guidelines, utilization management protocols, and case management are affecting individual treatment choices in ways that did not typically occur under traditional fee-for-service insurance arrangements. It is, therefore, likely that information regarding the economic efficiency of various treatments will play a growing role in structuring the administrative rules under which care is delivered. Given these developments, our findings support the use of structured pharmacological interventions in the management of uncomplicated depression in primary care. There is an economic rationale for initially prescribing an antidepressant medication when patients lack strong treatment preferences and there is no clinical contraindication. Furthermore, our results indicate that providing standardized treatments for primary care patients diagnosed with a major depression would be both clinically effective and cost-effective.

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REFERENCES

1. National Committee on Quality Assurance. *Health Plan Employer Data and Information Set, Version 3.0*. Washington, DC: National Committee on Quality Assurance; 1997.
2. American Managed Behavioral Health Association. *PERMS 2.0*. Washington, DC: American Managed Behavioral Health Association; 1997. 27261.
3. Foundation for Accountability. Available at: <http://www.faaact.org>. Accessed March 4, 1998.
4. Gold MR, Siegel JE, Russell LB, Weinstein MC. *Cost-Effectiveness in Health and Medicine*. New York, NY: Oxford University Press; 1996
5. *Clinical Practice Guideline Number 5: Depression in Primary Care 2: Detection and Diagnosis*. Rockville, Md: US Dept of Health and Human Services, Agency for Health Care Policy and Research; 1993. AHCPR publication 93-05501.
6. Schulberg HC, Block MR, Madonia MJ, Scott CP, Rodriguez E, Imber SD, Perel J, Lave JR, Houck PR, Coulehan JL. Treating major depression in primary care practice: eight-month clinical outcomes. *Arch Gen Psychiatry*. 1996; 53:913-919.
7. Schulberg HC, Madonia MJ, Block MR, Coulehan JL, Scott CP, Rodriguez E, Black A. Major depression in primary care practice. *Psychosomatics*. 1995;36: 129-137.
8. Schulberg HC, Block MR, Madonia MJ, Scott CP, Lave JR, Rodriguez E, Coulehan JL. The "usual care" of major depression in primary care practice. *Arch Fam Med*. 1997;6:334-339.
9. Hamilton, M. A rating scale for depression. *J Neurol Neurosurg Psychiatry*. 1960; 23:56-62.
10. Beck A, Ward C, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry*. 1961;4:53-63.
11. Brown C, Schulberg HC, Madonia MJ. Assessing depression in primary care practice with the Beck Depression Inventory and the Hamilton Rating Scale for depression. *Psychol Assess*. 1995;7:59-65.
12. Frank E, Prien RF, Jarrett RB, Keller MB, Kupfer DJ, Lavori PW, Rush AJ, Weissman MM. Conceptualization and rationale for consensus definitions of terms in major depression disorder: remission, recovery, relapse, and recurrence. *Arch Gen Psychiatry*. 1991;48:851-855.
13. Sackett DL, Torrance GW. The utility of different health states as perceived by the general public. *J Chronic Dis*. 1972;31 697-704.
14. Rubin HC, Patterson TL, Atkinson JH, Kaplan RM, Doch WL, McCutchar JA, Chandler JL, Grant I. Tracking effects of depression on life quality in HIV. Paper presented at the Second Conference on Biopsychosocial Aspects of HIV Infections; July 8, 1994; Brighton, England.
15. Kaplan RM. Using general measures of health related quality of life to assess mental health outcomes. In: Miller NE, Magruder KM, eds. *Cost-Effectiveness of Psychotherapy: A Guide for Practitioners, Researchers, and Policy-Makers*. New York, NY: John Wiley & Sons. In press.
16. Fryback DG, Dasbach EJ, Klein R, Klein BEK, Dorn N, Peterson K, Martin PA. The Beaver Dam health outcomes study: initial catalog of health state quality factors. *Med Decis Making*. 1993;13:89-102.
17. *1995 Redbook*. Montvale, NJ: Medical Economics Data, Inc; 1995.
18. Mumford E, Schlesinger HJ, Glass GV, Patrick P, Cuedron T. A new look at evidence about reduced cost of medical utilization following mental health treatment. *Am J Psychiatry*. 1984;14:1145-1158.
19. Borus JF, Olendzki MC, Kessler L, Burns BJ, Brandt UC, Broverman CA, Henderson PR. The offset effect of mental health treatment on ambulatory medical care utilization and charges. *Arch Gen Psychiatry*. 1985;42:573-580.
20. State of Arizona, Office of the Auditor General. *Performance Audit*. Phoenix, Ariz: Dept of Health Services, Division of Behavioral Health Services; December 1996. Report 96-19.
21. Bearegard KP, Cunningham P, Cornelius L. *Access to Health Care: Findings From the Survey of American Indians and Alaska Natives: National Medical Expenditure Survey Findings 9*. Rockville, Md: US Dept of Health and Human Services, Agency for Health Care Policy and Research; 1991. AHCPR publication 91-0028.
22. US Bureau of the Census. *Census of Population and Housing: 1990*. Washington, DC: US Bureau of the Census.
23. Gibbons R, Hedeker D, Elkin I, Watermaux C, Kraemer HC, Greenhouse JB, Shea MT, Imber SD, Sotsky SM, Watkins JT. Some conceptual and statistical issues in analysis of longitudinal psychiatric data. *Arch Gen Psychiatry*. 1993; 50:739-750.
24. Mullahy J, Manning WG. Statistical issues in cost effectiveness analysis. In: Sloan F, ed. *Valuing Health Care: Costs, Benefits and Effectiveness of Pharmaceuticals and Other Medical Technologies*. New York, NY: Cambridge University Press; 1994:149-184.
25. Manning WG, Fryback DG, Weinstein MC. Reflecting uncertainty in cost-effectiveness analysis. In: Gold MR, Siegel JE, Russell LB, Weinstein MC, eds. *Cost-Effectiveness in Health and Medicine*. New York, NY: Oxford University Press; 1996:247-276.
26. Parkerman H, Broadhead W, TSE C. The Duke Severity of Illness Checklist (DUSOI) for measurement of severity and comorbidity. *J Clin Epidemiol*. 1993; 46:379-393.
27. Stewart AL, Hays RD, Ware JE. The MOS Short-Form General Health Survey. *Med Care*. 1988;26:724-735.
28. Laupacis A, Fenny D, Detsky AS, Tugwell PX. How attractive does a new technology have to be to warrant adoption and utilization? tentative guidelines for using clinical and economic evaluations. *Can Med Assoc J*. 1992;146:473-481.
29. Meltzer, D. Accounting for future costs in medical cost-effectiveness analysis. *J Health Econ*. 1997;16:33-64.
30. Sturm R, Wells KB. How can care for depression become more cost-effective? *JAMA*. 1995;273:51-58.
31. Von Korff M, Katon W, Bush T, Lin EHB, Simon GE, Saunders K, Ludman E, Walker F, Unutzer J. Treatment costs, cost offset and cost effectiveness of collaborative management of depression. *Psychosom Med*. 1998;60:143-149.
32. Simon GE, Von Korff M, Heiligenstein JH, et al. Initial antidepressant choice in primary care. *JAMA*. 1996; 275:1897-1902.
33. Grof P. Designing long-term clinical trials in affective disorders. *J Affect Disord*. 1994;30:243-255.
34. Heckman JJ, Smith JA. Assessing the case for social experiments. *J Econ Perspectives*. 1995;9:85-110.
35. Lave JR, Schulberg HC. Integrating cost-effectiveness analyses within clinical trials of treatment for major depression in primary care practice. In: Miller NE, Magruder KM, eds. *Cost-Effectiveness of Psychotherapy: A Guide for Practitioners, Researchers, and Policy-Makers*. New York, NY: John Wiley & Sons. In press.