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A Cost-Effectiveness Analysis of Cognitive Behavior Therapy and Fluoxetine (Prozac) in the Treatment of Depression

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Depression affects at least 11 million Americans per year and costs the U.S. economy an estimated 44 billion dollars annually. Comprehensive review of the existing scientific evidence suggests that psychotherapy, particularly cognitive behavior therapy (CBT), is at least as effective as medication in the treatment of depression, even if severe (Antonuccio, Danton, & DeNelsky, 1995). These conclusions hold for both vegetative and social adjustment symptoms, especially when patient-rated measures are used and long-term follow-up is considered. In addition, several well-controlled studies with long-term follow-up (Evans et al., 1992; Shea et al., 1992; Simons, Murphy, Levine, & Wetzel, 1986) suggest that CBT may be more effective than drug treatment at preventing relapse. The relative effectiveness of psychotherapy for depression, particularly CBT, has been reinforced by meta-analyses reported in both psychiatry (Hollon, Shelton, & Loosen, 1991; Wexler & Cicchetti, 1992) and psychology journals (Dobson, 1989; Robinson, Berman, & Neimeyer, 1990; Steinbrueck, Maxwell, & Howard, 1983). In the era of managed care, it is not enough to be effective; treatments must be cost-effective. This paper considers the outcome studies as the basis for a cost-effectiveness comparison of drugs and psychotherapy in the treatment of unipolar depression. The analysis shows that over a 2-year period, fluoxetine alone may result in 33% higher expected costs than individual CBT treatment and the combination treatment may result in 23% higher costs than CBT alone. Supplemental analysis shows that group CBT may only result in a 2% ($596) cost savings as compared to individual treatment.

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The point prevalence of unipolar depression is estimated to be between 3% and 13%, with 20% to 50% of the adult population having a prior history, and as much as 20% experiencing at least some depressive symptoms at any given time (Amenson & Lewinsohn, 1981; Kessler et al., 1994; Oliver & Simmons, 1985). Women are consistently found to have rates of depression twice as high as men. In 1990, at least 11 million Americans experienced an episode of depression, costing the U.S. economy an estimated $44 billion in increased accident rates, increased substance abuse, increased medical hospitalization, and increased somatic illnesses and outpatient medical utilization (Greenberg, Stiglin, Finkelstein, & Berndt, 1993). Antidepressant drug treatment (Morris & Beck, 1974) and cognitive behavior therapy (CBT; Antonuccio, Ward, & Tearnan, 1989) are empirically based treatments for depression that have established clinical efficacy (Antonuccio, Danton, & DeNelsky, 1995). In the era of managed care and limited resources, depression treatments must demonstrate their cost-effectiveness as well as their clinical effectiveness. The current paper addresses the relative clinical effectiveness and cost-effectiveness of drugs and CBT in the treatment of unipolar depression. The comparative outcome literature is briefly reviewed. A cost-effectiveness model, previously generated from this outcome literature (Antonuccio, Thomas, & Danton, in press) is modified to evaluate the comparative cost-effectiveness of individual CBT, fluoxetine, and combination protocols.

Clinical Outcome of CBT Compared With Pharmacotherapy

One approach to treating depression involves addressing the cognitions that mediate the emotional impact of events in patients' lives (e.g., Beck, Rush, Shaw, & Emery, 1979; Beck & Young, 1985). The proponents of this approach assert that it is not necessarily aversive events that lead to depression, but rather cognitions about those events. CBT involves helping patients modify cognitive distortions that may be negatively impacting mood.

Many studies have shown cognitive therapy to be more effective than antidepressant medication (Blackburn, Bishop, Glen, Whalley, & Christie, 1981; Evans et al., 1992; Kovacs, Rush, Beck, & Hollon, 1981; Rush, Beck, Kovacs, & Hollon, 1977; Rush, Beck, Kovacs, Weissenburger, & Hollon, 1982). Some studies have shown cognitive therapy alone to be as effective as antidepressant medication (Elkin et al., 1989; Hollon et al., 1992) or combined cognitive/drug treatment (Beck, Hollon, Young, Bedrosian, & Budenz, 1985; Blackburn et al., 1981; Covi & Lipman, 1987; Evans et al., 1992; Hollon et al.; Murphy, Simons, Wetzel, & Lustman, 1984). Yet other studies suggest that cognitive therapy adds to the efficacy of standard antidepressant drug treatment (Bowers, 1990; Dunn, 1979; Miller, Norman, Keitner, Bishop, & Dow, 1989; Teasdale, Fennell, Hibbert, & Amies, 1984).

Other studies have evaluated CBT treatments that emphasize the behavioral aspects (e.g., social skills and pleasant activities) of depression. Some studies found such behavioral interventions are more effective than medica-

tion alone (McLean & Hakstian, 1979; Miller et al., 1989), are as effective as combined treatment (Hersen, Bellack, Himmelhoch, & Thase, 1984; Stravynski et al., 1994; Wilson, 1982), or add to the efficacy of standard drug treatment with drug-refractory depression (Antonuccio et al., 1984). One study (Roth, Bielski, Jones, Parker, & Osborn, 1982) found that adding antidepressant medication to such a behavioral intervention speeded recovery somewhat, but the outcomes were equivalent at treatment termination.

Finally, the preponderance of the evidence suggests that drug treatments do less well than CBT during follow-up (e.g., Blackburn, Eunson, & Bishop, 1986; Evans et al., 1992; Hersen et al., 1984; Hollon, Shelton, & Loosen, 1991; Kovacs et al., 1981; McLean & Hakstian, 1990; Rush et al., 1977; Shea et al., 1992), and are not more effective than psychotherapy with endogenous (Blackburn et al., 1981; Greenberg, Bornstein, Greenberg, & Fisher, 1992a; Zimmerman & Spitzer, 1989), severe (Hollon et al., 1992; McLean & Taylor, 1992; Shea et al.), chronic (Rush, Hollon, Beck, & Kovacs, 1978), or inpatient (Brugha, Bebbington, MacCarthy, Sturt, & Wykes, 1992) depression.

Continuation Drug Treatment

Some investigators have argued that the relatively high relapse rate after drug treatment indicates that depression should be treated like a chronic medical disease, requiring ongoing, long-term, high dose medication treatment indefinitely (e.g., Frank et al., 1990; Kupfer et al., 1992; Paykel, Dimascio, Haskell, & Prusoff, 1975; Reynolds et al., 1992). This logic is problematic: Drug treatment results in a higher relapse rate than CBT, therefore, patients should be maintained on drugs to prevent relapse. These maintenance studies typically rely on clinician ratings of outcome, and all patients are initially given combined treatment or drug treatment only. The maintenance phase of treatment is conducted only with the responders. Since psychotherapy alone is not offered to patients initially, the maintenance phase of treatment is essentially restricted to drug responders and those patients who can tolerate the side effects. Therefore, the patient samples in these drug maintenance studies should not be considered representative of the general population of depressed patients.

A notable exception is a well-controlled study with 2 years of follow-up evaluating the impact of continuing medication (Evans et al., 1992; Hollon et al., 1992). These investigators randomly assigned 107 nonpsychotic, nonbipolar depressed patients to 12 weeks of cognitive therapy alone, imipramine hydrochloride alone (mean of 232 mg/day with plasma levels at least 180 ng/ml), or combined treatment. A total of 64 patients completed treatment with no differential attrition. CBT and pharmacotherapy did not differ in terms of symptomatic response on patient-rated or clinician-rated measures, even among severely depressed patients. Initial severity predicted poorer response within the pharmacotherapy condition but not within CBT. The combined treatment was not significantly more effective than the single treatments. Two patients committed suicide with study medication and a

third patient made a nonlethal attempt. Two other patients were withdrawn from pharmacotherapy alone because of severe suicidal risk. Three other patients were withdrawn from pharmacotherapy alone because of severe side effects. A total of 10 patients, all in the pharmacotherapy alone condition, failed to complete treatment due to medication side effects, a statistically significant result.

During follow-up, half of the patients treated with pharmacotherapy alone continued to receive study medications for the first year of follow-up. Among patients showing at least partial response, patients previously treated cognitively (with or without medications) showed a significantly lower relapse rate compared to imipramine patients from whom medications were withdrawn. Thus, patients treated with 3 months of CBT (either alone or in combination with medications) had less than half the relapse shown by patients who received 3 months of medication alone. The relapse rate after 3 months of CBT did not differ from that of patients provided with 15 months of medication. If suicide, side effects, and relapse rates are considered, these data suggest that treating depression with brief CBT can be more cost-effective than long-term drug treatment.

Future studies need to also investigate whether, or how much, relapse might be further reduced if continuation CBT is offered. A preliminary investigation showed that when recovered drug treatment patients have CBT added to their drug regimen, they have a substantially lower relapse rate (35%) compared with routine clinical management (70%) over a 4-year period during which the medications are gradually discontinued (Fava, Grandi, Zielezny, Rafanelli, & Canestrari, 1996).

Meta-analytic Comparisons of Drugs vs. Psychotherapy

Several meta-analyses have been conducted involving multiple studies with thousands of depressed patients. These meta-analyses have found (a) psychotherapy had outcome that was comparable (Hollon et al., 1991; Robinson et al., 1990) or better (Dobson, 1989; Steinbreuck, Maxwell, & Howard, 1983) than pharmacotherapy alone, (b) combined psychotherapy and drug treatment does not appear to be clearly superior to either therapy alone (Conte, Plutchik, Wild, & Karasu, 1986; Hollon et al.; Robinson et al., 1990), (c) when dropout rate is considered, pharmacotherapy alone has substantially worse outcome than psychotherapy alone or combined treatment (Wexler & Cicchetti, 1992), and (d) treatment with cognitive therapy (with or without drugs) during the acute episode appears to reduce the risk of subsequent relapse following termination (Hollon et al.).

The study by Wexler and Cicchetti (1992) involved a meta-analysis of treatment success rates, treatment failure rates, and treatment dropout rates from 7 well-controlled studies ($N = 513$) comparing psychotherapy and medication for depression. They concluded that combined treatment offers no advantage over treatment with psychotherapy alone and only modest advantage over treatment with pharmacotherapy alone. They suggest that psycho-

therapy alone should usually be the initial treatment for depression rather than exposing patients to unnecessary costs and side effects of combined treatment. When dropout rate is considered together with treatment success rates, the pharmacotherapy alone condition is substantially worse than psychotherapy alone or the combined treatment. Their review suggests that in a hypothetical cohort of 100 patients with major depression, 29 would recover with pharmacotherapy alone, 47 would recover if given psychotherapy alone, and 47 would recover if given combined treatment. Negative outcomes (i.e., dropouts or no response) would occur in 52 pharmacotherapy patients, 30 psychotherapy patients, and 34 combined patients. Comorbid personality disorder and substance abuse may further decrease treatment response (Wexler & Nelson, 1993).

In summary, several meta-analyses, reported in both psychiatry and psychology journals, covering multiple studies with thousands of patients, are remarkably consistent in supporting the perspective that psychotherapy is at least as effective as medication in the treatment of depression. These conclusions hold for both vegetative and social adjustment symptoms, especially when patient-rated measures are used and long-term follow-up is considered. Though there is some overlap of included studies, all of these meta-analyses were conducted independently. Except for the meta-analyses of Dobson (1989) and Hollon et al. (1991), which used only studies including cognitive behavioral interventions, the other meta-analyses combined all brands of psychotherapy for depression. This may obscure differences in outcome between the different brands of treatment. Different types of psychotherapy may have different outcomes (e.g., McLean & Hakstian, 1979). It should also be noted that Robinson et al. (1990) found psychotherapy outcomes to be robust on both self-report and clinician measures. In contrast, antidepressant drugs have not fared well compared with control conditions on patient-rated measures (Greenberg, Bornstein, Greenberg, & Fisher, 1992b), and serious questions about the integrity of the placebo double blind have been raised (Greenberg & Fisher, 1989). Despite the foregoing evidence to the contrary, the conventional wisdom in medicine, among the lay public, in the media, and even within the mental health profession, continues to be that drugs are more effective and less expensive than psychotherapy for depression (e.g., Kramer, 1993), and that the combination treatment is superior to either one alone. There is also a tendency to minimize the side effects of antidepressant drugs.

Side Effects

One of the costs of medications that may be underappreciated involves side effects. Research suggests that antidepressants are the most common agent used in suicide by poisoning (Kapur, Mieczkowski, & Mann, 1992) and have been involved in as many as one-half of serious adult overdoses (Kathol & Henn, 1982). We are aware of no data about the relative risk of suicide in patients treated with drugs compared with those treated with psychotherapy.

Although a suicidal patient treated with psychotherapy may commit suicide, the treatment itself does not become the cause of death.

The side effects, some potentially quite serious, associated with the tricyclic antidepressants are detailed elsewhere (Antonuccio et al., 1995). So far, fluoxetine (Prozac) and the other selective serotonin-reuptake inhibitors (SSRIs) appear to be a safer alternative to the tricyclic antidepressants. Although they appear to have about the same risk of overdose, death appears to be a less likely outcome with the SSRIs (Kapur et al., 1992). While the newer SSRIs may be safer when used alone, there are data to suggest that, when combined with other medications, they are more dangerous due to their pharmacodynamic and pharmacokinetic properties (e.g., Nemeroff, DeVane, & Pollock, 1996; Settle, 1992). For example, at therapeutic doses, they can be lethal when combined with Monoamine-Oxidase Inhibitors (MAOIs; Settle). Given the common use of multiple concurrent medications, it is not clear that the newer antidepressants will actually result in safer outcomes. Even when used alone, fairly common side effects of the SSRIs include agitation, sleep disruption, nausea, and sexual problems (Settle). They can also increase the risk of miscarriage and neonatal complications if used during the first trimester (Pastuszak et al., 1993), a significant concern given that 70% of the antidepressants are prescribed for women (Olfson & Klerman, 1993), many of child-bearing age. For a minority of patients, these new medications also appear to carry a significant risk for suicide induction, mania, akathisia, and extrapyramidal effects (Lenhoff, 1994).

Though side effects are important "costs" to consider, it is difficult to quantify them for inclusion in a cost-effectiveness model. It is especially difficult to quantify the physical, emotional, and social consequences of side effects for which patients do not seek medical treatment.

Establishing a Cost-Effectiveness Model

Yates (1995) described several models for measuring cost-effectiveness and cost-benefit in clinical research and for optimizing cost-effectiveness and cost-benefit in clinical practice. Traditional research only looks at how procedures are implemented and to what extent they lead to certain outcomes. Cost-effectiveness analyses add data on treatment costs to find the least expensive way to achieve certain outcomes or the most effective way to deliver services within budget constraints.

The model begins with an analysis of the comparative treatment costs on three levels: the direct treatment costs to the patient or third party provider, direct costs to the community (e.g., from lost wages, etc.), and indirect costs to society (e.g., lost productivity). By considering all three types of depression costs, a socio-economic model results. Table 1 shows that, based on this model, drug treatment is 75% more expensive than CBT alone when direct costs to the patient and third party payer costs are considered. The combination treatment is 101% more expensive than CBT alone. When costs to the

TABLE 1
COMPARATIVE COST ANALYSIS OF DEPRESSION TREATMENTS

	Total Costs by Treatment Type for 2-Year Treatment Plan			Cost Differences Compared to CBT	
	Individual CBT	Fluoxetine	Combination	Fluoxetine	Combination
Direct patient/third party provider costs					
Health care provider charges	$2,000	$1,120	$2,800	<$880>	$800
Medication	0	3,629	3,629	3,629	3,629
Lost wages	334	214	356	<120>	22
Travel costs	60	72	84	12	24
Comorbidity costs	4,874	7,703	7,703	2,830	2,830
Total costs to the patient/third party provider	$7,268	$12,738	$14,572	$5,470	$7,305
Percentage cost difference from CBT				75%	101%
Direct costs to the community					
Economic multiplier effect from lost wages	$718	$459	$766	<$258>	$48
Reduced taxes due to lost wages	136	87	145	<49>	9
Reduced community service work by patients	400	400	400	0	0
Total costs to the community	$1,253	$946	$1,310	<$307>	$57
Percentage cost difference from CBT				<25%>	5%
Indirect costs to society					
Lost productivity during treatment	$3,729	$4,256	$3,781	$527	$53
Economic multiplier effect from lost productivity	8,017	9,150	8,130	1,133	113
Reduced taxes due to lost productivity	1,516	1,730	1,537	214	21
Lost income potential from suicide	1,913	1,913	1,913	0	0
Total costs to society	$15,174	$17,049	$15,362	$1,874	$187
Percentage cost difference from CBT				12%	1%
TOTAL TREATMENT COSTS	$23,696	$30,733	$31,245	$7,038	$7,549
Percentage cost difference from CBT				30%	32%

community and costs to society are considered, the total treatment costs for fluoxetine alone and combination treatment are 30% and 32% more expensive than for CBT, respectively.

Method of Quantifying Costs

Table 1 provides the treatment costs used in Tables 2 through 4. Assumptions and data for each line item of cost in Table 1 follow.

Health Care Costs

In the model, all treatments are delivered over a 2-year period. It is assumed that CBT is delivered weekly for 15 weeks followed by 5 booster sessions over the remaining period. CBT sessions are costed at $100 per individual session. Fluoxetine is costed at $2.49 per 20 mg pill. It is assumed that the typical patient will take 2 pills per day and see a psychiatrist at least once every 6 weeks. It is assumed a psychiatrist charges $70 for a typical 30-minute outpatient medication management visit.

The combination treatment is assumed to comprise 20 1-hour sessions delivered in the same pattern as the CBT alone treatment. The assumption is made that the patient sees a psychiatrist individually who can prescribe the medication and provide the CBT in the combined treatment. It is assumed that the medication treatment is woven into the session. For the combination treatment, it is assumed that the prescription is phoned into the pharmacy when needed between therapy sessions so no extra trips to the doctor are required. The psychiatrist is assumed to charge $140 per session in the combined treatment (i.e., double the half-hour rate). All three treatment protocols are based on models described in the studies reviewed in this paper.

Quantifying Lost Wages and Travel Costs

The opportunity cost (i.e., the differential money that could have been made by doing something else) for patients who receive treatment is assumed to be $8.90 per hour. This is the after-tax net pay based on a $15 per hour gross wage rate. It is assummed the average CBT individual session is 1 hour. It is assumed that the average medication check with a psychiatrist lasts about 30 minutes. It is assumed that prescriptions are filled on site or after work if they are purchased at an off-site pharmacy. It is assumed that it takes 1 hour to get to and from all appointments. The 1995 IRS mileage rate of 30 cents per mile is used. The average round-trip to the doctor is assumed to be 10 miles while a round-trip to the pharmacy is assumed to be 5 miles.

Quantifying Comorbidity Costs

Simon, VonKorff, and Barlow (1995) reported 1992 HMO medical costs for depressed and nondepressed patients. Depressed patients had a mean of $1,875 higher health care costs overall compared to nondepressed matched controls. Less than 20% of the difference between depressed and nondepressed patients was due to mental health costs. Among depressed patients treated with anti-

depressant drugs, the mean total health care costs were $2,035 higher than those for comparable nondepressed patients. Nonmedicated depressed patients had a mean of $1,287 higher health care costs than those for the comparison group. Cost differences between depressed and nondepressed patients are multiplied by 80% to negate the direct costs of mental health treatments. The cost differences are adjusted to current retail prices paid by patients or third party payers. It is assumed that some of the costs of side effects are captured here when patients seek treatment for their side effects, resulting in higher overall treatment costs. To the extent that patients do not seek treatment for side effects, comorbidity costs for antidepressants are underestimated.

Evaluating the Impact of the Economic Multiplier and Taxes

An economic multiplier measures the effect on the economy from spending $1.00 of household income. We used the Nevada state household spending multiplier as of 6-21-96. Household income is the net pay brought home by the income earners. Since the economic multiplier applies to net pay, it does not consider the effect of taxes from paychecks. Therefore, the lost taxes are separately calculated (federal and state income taxes at 28% and 5%, social security at 7.65%).

Quantifying Community Service Costs

We assumed the average adult donates 40 hours per year to community service. We also assumed the cost of providing these services, if not donated, is $10 per hour. We also assumed that depression causes a 50% reduction in donated time across all treatments.

Quantifying Lost Productivity During Treatment

Greenberg et al. (1993) estimated that 7.8 million workers lost 290 million workdays in 1990 due to depression. This is 37 workdays per year per patient. We assumed an unrecovered patient loses 37 days per year during the 2-year period under consideration. It is assumed a recovered patient loses half that amount (18.5 days) and a partially recovered patient loses something in the middle, about 27.75 workdays. An expected number of days lost was calculated for a typical patient from each of the three treatments. The number of expected days lost was then multiplied by the average net wage rate.

Quantifying Lost Income Potential From Suicide

In 1990, there were an estimated 11 million depressed Americans, resulting in 18,400 suicides (Greenberg et al., 1993). Those suicides resulted in a lost income potential of $7.5 billion dollars for an average of $407,609 per suicide for $681.81 per depressed person. Adjusting for inflation, this is $1,913 per 2-year treatment period per depressed patient in lost income potential from suicide. Costs to society from suicide are posttreatment costs, and are estimated to be the same for all depressed patients regardless of treatment type.

The raw data used in this model are presented in Appendix B.

Establishing Treatment Outcome Distribution

The Table 1 model is still incomplete. It needs to be expanded into an expected costs model. The expected treatment cost includes probability distributions associated with each treatment for the following events: (1) the expectation of treatment success, partial success, and failure, (2) the expectation that a certain percentage of patients will relapse, and (3) the expectation of subsequent treatments if the first treatment is not successful. Based on the outcome data from the Wexler and Cicchetti (1992) meta-analysis and the long-term outcome studies described in this paper, an estimate can be made regarding the percentage of patients who will recover, partially recover, remain depressed, drop out, or relapse in each of the three treatment options. All of the existing comparative studies use tricyclic antidepressants. Because the preponderance of the evidence suggests that SSRIs in general, and fluoxetine in particular, have similar efficacy (Greenberg, Bornstein, Zborowski, Fisher, & Greenberg, 1994) and overall dropout rates when compared to tricyclic antidepressants (Anderson & Tomenson, 1995; Song et al., 1993), the tricyclic outcome numbers from this comparative meta-analysis are used. Of those depressed patients who start drug treatment alone, it is estimated that 29% will recover, 19% will have partial success, 17% will not respond, and 35% will drop out (Wexler & Cicchetti). For CBT alone, it is estimated that 47% will recover, 23% will have partial success, 11% will not respond, and 19% will drop out. For the combined treatment, it is estimated that 47% will recover, 19% will have partial success, 8% will not respond, and 26% will drop out (Wexler & Cicchetti). These treatment outcome distributions are used in Tables 2 through 4.

Establishing Relapse Rates and Time Comparisons

It is estimated that roughly 27% of the recovered CBT patients will relapse, 59% of the recovered drug-only patients will relapse, and 29% of the recovered combined treatment patients will relapse (Evans et al., 1992; Shea et al., 1992; Simons, Murphy, Levine, & Wetzel, 1986). The average time to relapse could also be estimated from the studies reviewed. The average CBT patient who relapsed did so in about 12.1 months. Relapsing drug-only patients took an average of 6.6 months. The average combination patient who relapsed did so in 9.6 months. Relapse costs are based on how much longer patients will experience depression in the drug and combination conditions (due to earlier relapse) compared with the CBT condition. All of the treatment studies looked at relapse in the recovered patients only. To illustrate how relapse rates and times are incorporated in this model, consider Table 3 (line 2). Of the 29% of patients responding to fluoxetine treatment, it was estimated that 59% will relapse 5.5 months sooner than patients receiving CBT. A monthly "posttreatment cost to society" for depressed patients was calculated for all treatments ($1,230/month) by considering lost productivity, its economic and tax effects, comorbidity, and lost income from suicide potential.

TABLE 2
CALCULATION OF INDIVIDUAL CBT EXPECTED TREATMENT COSTS

Patient's expected outcome	Percentage of patients				Expected cost
Treatment success	47%	×	$23,696	Treatment cost	= $11,137
	47%	×	27%	Relapsing × $1,230 Post-treatment cost to society × 0 months relapsed	= 0
Partial success	23%	×	$23,696	Treatment cost	= 5,450
	23%	×	0.5	Post-treatment cost to society of $1,230 × 12.1 month relapse period	= 1,712
Failures	11%	×	$23,696	Treatment cost	= 2,607
	11%	×	$1,230	Post-treatment cost to society × 12.1 month relapse period	= 1,638
Drop-outs	19%	×	$5,109	Partial treatment cost	= 971
	19%	×	$1,230	Post-treatment cost to society × 17.42 months to end of 2-year treatment period	= 4,072
Sum	100%				
Subsequent treatment	31%	×	$988	Treatment cost	= 306
CBT EXPECTED TREATMENT COST					$27,892

TABLE 3
CALCULATION OF FLUOXETINE EXPECTED TREATMENT COSTS

Patient's expected outcome	Percentage of patients					Expected cost
Treatment success	29%	×	$30,733	Treatment cost	=	$8,913
	29%	×	59%	Relapsing × $1,230 Post-treatment cost to society × 5.5 months relapsed	=	1,158
Partial success	19%	×	$30,733	Treatment cost	=	5,839
	19%	×	0.5	Post-treatment cost to society of $1,230 × 12.1 month relapse period	=	1,414
Failures	17%	×	$30,733	Treatment cost	=	5,225
	17%	×	$1,230	Post-treatment cost to society × 12.1 month relapse period	=	2,531
Drop-outs	35%	×	$3,891	Partial treatment cost	=	1,362
	35%	×	$1,230	Post-treatment cost to society × 18.89 months to end of 2-year treatment period	=	8,135
Sum	100%					
Subsequent treatment	57%	×	$4,281	Treatment cost	=	2,440
FLUOXETINE EXPECTED TREATMENT COST						$37,017

TABLE 4
CALCULATION OF COMBINATION EXPECTED TREATMENT COSTS

Patient's expected outcome	Percentage of patients			Expected cost
Treatment success	47% ×	$31,245	Treatment cost	= $14,685
	47% ×	29%	Relapsing × $1,230 Post-treatment cost to society × 2.5 months relapsed	= 419
Partial success	19% ×	$31,245	Treatment cost	= 5,936
	19% ×	0.5	Post-treatment cost to society of $1,230 × 12.1 month relapse period	= 1,414
Failures	8% ×	$31,245	Treatment cost	= 2,500
	8% ×	$1,230	Post-treatment cost to society × 12.1 month relapse period	= 1,191
Drop-outs	26% ×	$5,020	Partial treatment cost	= 1,305
	26% ×	$1,230	Post-treatment cost to society × 20.17 months to end of 2-year treatment period	= 6,451
Sum	100%			
Subsequent treatment	44% ×	$988	Combination treatment cost	= 435
COMBINATION EXPECTED TREATMENT COST				$34,337

For the purposes of this model, we have assumed that partially recovered patients don't relapse but they incur half the costs to society of a depressed patient during the time period under investigation.

Quantifying Dropout Treatment Costs

Dropout costs were also calculated based on an estimate of the average time to drop out from the reviewed studies. The average CBT dropout patient quit treatment after 6.58 months. The relative times to drop out in drug-only and the combination treatment were 5.11 months and 3.83 months respectively. To illustrate how this is included, consider Table 2 (Drop-outs, line 2). Dropping out after 6.58 months, a depressed person will incur $1,230 per month in "posttreatment costs to society" for the remaining 17.42 months of the 2-year treatment plan.

Establishing Subsequent Treatment Rates

Kovacs et al. (1981) found that of all patients starting treatment, 50% of CBT patients and 76% of drug patients will reenter treatment. Shea et al. (1992) found that 12% of recovered CBT patients and 37% of recovered pharmacotherapy patients return to treatment during follow-up. We assumed the average of these return rates for relapsed patients, 31% for CBT and 57% for drugs alone. Because there are no data to guide us about the return rates for combination patients, we assumed the average return rate (44%) for the combination condition. Based on our analysis of Shea et al., of the relapsed CBT patients who return to treatment, 28% will seek CBT, 29% will seek drug treatment, and 43% will seek "any" treatment (assumed to be the average of the three treatment costs). Of the relapsed drug-only patients who return to treatment, 33% will seek CBT, 29% will seek drug treatment, and 38% will seek "any" treatment. The length of subsequent treatment following CBT and drug-only treatment was 4.2 weeks and 20.3 weeks respectively (Shea et al.). Subsequent treatment duration and rates for the combination treatment were assumed to be equivalent to the CBT condition.

Group vs. Individual CBT Treatments

As a subsidiary analysis, we finally considered the comparative costs of group versus individual CBT treatment. A priori, one would expect that group treatment should be much less costly than individual CBT. Surprisingly, this is not supported by the model, however, as shown in Table 5.

While individual CBT sessions are costed at $100 per 1-hour session, current group rates are $30 for a 2-hour session. As shown in Appendix A, this results in a group CBT "direct patient/third party provider cost" of $6,351, a savings of $917 over individual session costs. However, because group sessions are twice as long, a greater "direct cost to the community" results from the extra lost wages ($342 difference between Appendix A and Table 1 amounts). When expected costs (Tables 2–4) are recalculated for group sessions, only a 2% cost decrease results ($596 in Table 5) if group CBT treat-

TABLE 5
COMPARISON OF SOCIO-ECONOMIC COSTS

	CBT	Fluoxetine	Combination
Individual Treatment			
Treatment costs	$23,696	$30,733	$31,245
Cost difference from CBT		$7,038	$7,549
Percentage difference from CBT		30%	32%
Total expected treatment costs	$27,892	$37,017	$34,337
Cost difference from CBT		$9,125	$6,445
Percentage difference from CBT		33%	23%
Group Treatment			
Treatment costs	$23,120	$30,733	$31,245
Cost difference from CBT		$7,613	$8,125
Percentage difference from CBT		33%	35%
Total expected treatment costs	$27,296	$36,867	$34,308
Cost difference from CBT		$9,571	$7,012
Percentage difference from CBT		35%	26%
Group vs. Individual Cost Savings			
Treatment costs			
Cost difference (individual − group)	$576	$0	$0
Percentage difference	2%		
Total expected treatment costs			
Cost difference (individual − group)	$596	$150	$29
Percentage difference	2%	0%	0%

ment is replaced with individual treatment. Though there is some evidence that group and individual CBT have comparable outcomes (e.g., Brown & Lewinsohn, 1984; Miller & Berman, 1983), future research is necessary to address the comparative cost benefit (i.e., clinical effectiveness-to-cost difference). As an aside, when group CBT becomes an option in subsequent treatments, a small cost reduction results for fluoxetine and combination treatments ($150 and $29 respectively, in Table 5).

Cost Trade-Offs to Equate Treatments

This research study sought to accomplish two goals: (1) developing a model to compare the socio-economic costs of various treatments, and (2) using this model to compare treatment options. With respect to the second goal, the outcome from these comparisons depends on the underlying data used in the model. Thus, we wanted to investigate the effect on comparative costs from changing the data and assumptions. For example, questions about the hourly rates and costs of medication first come to mind.

To equate expected treatment costs, the differences reported in Table 5 have to be eliminated. To illustrate this, the expected treatment cost of fluoxetine is $9,125 greater than CBT (from the "Individual treatment, Total expected

treatment costs, Cost difference from CBT" line). Now consider fluoxetine and the associated health care provider costs shown in the first two lines of Table 1. If both the medication and treatment are provided at no cost, only $4,749 ($1,120 + $3,629) of the Table 1 treatment cost difference is eliminated. Recalculating the expected costs in Table 3 reduces the expected cost difference in Table 5 to $4,509. In other words, fluoxetine would still be more costly than CBT (by 16%).

Conversely, if CBT treatments are provided at no cost, only $2,000 (from Table 1) of the cost difference is eliminated. While health care provider charges and medication are significant variables in this model, totally eliminating them from the model will not change the conclusion that CBT is a more cost-effective treatment than fluoxetine. Eliminating these costs from Table 1, fluoxetine would still be $6,860 (27%) more costly than CBT in Table 5.

The only way to equate the expected costs of CBT and fluoxetine by manipulating these two variables is through some unrealistic or unethical combination. For example, not changing the original Table 1 fluoxetine costs, the expected treatment costs are about equal if the hourly charge for CBT is increased to $502 per session. At the other extreme, if fluoxetine and its associated treatment costs are free, the hourly CBT rate must increase to $438 before the treatment costs are equal.

It appears that the comparative cost difference is primarily caused by three variables: medication costs (Table 1), comorbidity costs (Table 1), and clinical success probabilities (Tables 2–4). Realistically, for fluoxetine to become as cost-effective as CBT, simultaneous changes will be needed. For example, generic substitutes for fluoxetine can reduce medication costs. Supplemental medication and improved therapy protocols may reduce comorbidity costs and increase the fluoxetine treatment success rate. Thus, the model is also useful in identifying fertile areas for future research. Inputting such projected changes into the model will allow us to assess the utility of this research. To illustrate, assume that fluoxetine cost is reduced to $1.00 per pill, a new drug is developed that reduces comorbidity to $2,000, and in combination with improved therapy protocols, the clinical success rate is increased from 29% to 50% (with respective changes in partial success, failures, dropouts, relapses, and subsequent treatments to: 35%, 10%, 5%, 10%, and 10%). Inputting the new data into the model would result in fluoxetine becoming as cost-effective as CBT alone.

Other Considerations

Because two of the authors practice CBT, a special attempt was made to bias against CBT in terms of costs wherever judgment was involved. For example, in the outcome studies of CBT, the treatment is usually delivered in 10 to 20 sessions over a period of 3 or 4 months. The average number of sessions in these studies is actually about 12 to 15. We purposely chose 20 sessions of CBT delivered over the 2-year period, which is likely to inflate

the cost of CBT somewhat. All of the comparison studies offered a comparable number of drug sessions to match treatment intensity of the CBT. We purposely chose less frequent and less intense drug treatment in this analysis to reflect real-world practices. The costs for drug treatments in our model are therefore likely to be less than the actual costs in most of the treatment outcome studies we reviewed. There is also some evidence that CBT can be delivered rather effectively in the form of a self-help manual (Jamison & Scogin, 1995). Such an option was not considered in our model. If it were, it would reduce the direct cost of CBT treatment considerably. The CBT outcome numbers inferred from the Wexler and Cicchetti (1992) meta-analysis are likely to underestimate actual CBT outcome because that meta-analysis included the inferior outcome for the insight-oriented psychotherapy from McLean and Hakstian (1979). Also, our model does not incorporate recent data indicating that health insurance costs increase for those who have a history of fluoxetine use (Protos, 1995). Finally, we were unable to develop a way to quantify the costs of untreated side effects. Such costs are extremely important and are an issue for future consideration. It is quite likely that if side effects were somehow quantified, they would overwhelm the model, with even greater advantages accruing to CBT.

Conclusions

As can be seen in Table 5, this model projects CBT as the most cost-effective treatment, followed by combined treatment, followed by fluoxetine alone. Over the 2-year period under evaluation, it is estimated that fluoxetine alone will result in 33% higher expected cost than individual CBT alone. It is estimated that the combination treatment will result in 23% higher costs than individual CBT alone. Based on this cost-effective model, CBT appears to be the treatment of first choice for unipolar depression. If the treatment fails, it can be supplemented by fluoxetine or another SSRI. Fluoxetine alone does not appear as cost-effective as the other two treatments. In this model, if fluoxetine is used, it is more cost-effective to use it in combination with CBT.

It is important to note that we are proposing a model of cost-effectiveness that relies on specific assumptions and numerical estimates drawn from the scientific literature. It is quite possible to debate the numerical values that are used for each of the cost variables (Appendix B). We have tried to incorporate available data on outcome, relapse, and dropout percentage—variables that may be overlooked in any analysis that considers only direct costs. The value of this analysis depends in part on how well the data from experimental studies generalize outside of academic settings. We hope we have generated a fairly comprehensive model that can be used by others to evaluate the costs and benefits of alternative treatments in other real-world settings.

All current published comparative studies compare tricyclic antidepressants and psychotherapy. We expect the numbers may change when studies

comparing CBT and fluoxetine are published, but it may take decades to generate an adequate database. In the meantime, there is no evidence that outcome with SSRIs is vastly different than that with tricyclics. Also, costs are not static. We expect the prices of medication and provider charges to change over time and vary with setting.

We have deferred any attempt to quantify the nonmedical costs of side effects. We encourage others to develop creative ways to quantify the costs associated with side effects so they can be incorporated into future models. Even though antidepressants are the most common agents used in suicide by poisoning, no attempt has been made to differentially quantify suicide for each treatment because there are no current data available to allow estimates of the relative risk of suicide for patients receiving CBT or fluoxetine.

Despite the outcome and cost data detailed in this paper, an estimated 48% of depressed patients are treated in the general medical sector, with a probable reliance on medication interventions (Narrow, Regier, Rae, Manderscheid, & Locke, 1993). These data and analyses suggest that treatment patterns for depression ought to be carefully reexamined. When long-term outcome for depression is considered, it appears that CBT may be more clinically effective and more cost-effective than antidepressant medication alone. If a particular patient does not respond to CBT, then the costs and benefits of other treatment options can be carefully weighed.

Finally, we would like to note that we do not consider cost-effectiveness to be the ultimate criterion by which treatment options ought to be evaluated. When loved ones become depressed, we are likely to want them treated with the most clinically effective interventions as long as the costs are not significantly higher than the alternative choices. Nevertheless, CBT alone appears to be an option that is both clinically effective and cost-effective, providing an easy choice.

APPENDIX A
COMPARISONS WITH GROUP CBT TREATMENT

	Total Costs by Treatment Type for 2-Year Treatment Plan			Cost Differences Compared to CBT	
	Group CBT	Fluoxetine	Combination	Fluoxetine	Combination
Direct patient/third party provider costs					
Health care provider charges	$950	$1,120	$2,800	$170	$1,850
Medication	0	3,629	3,629	3,629	3,629
Lost wages	467	214	356	<253>	<111>
Travel costs	60	72	84	12	24
Comorbidity costs	4,874	7,703	7,703	2,830	2,830
Total costs to the patient/third party provider	$6,351	$12,738	$14,572	$6,387	$8,222
Percentage cost difference from CBT				101%	129%
Direct costs to the community					
Economic multiplier effect from lost wages	$1,005	$459	$766	<$546>	<$239>
Reduced taxes due to lost wages	190	87	145	<103>	<45>
Reduced community service work by patients	400	400	400	0	0
Total costs to the community	$1,595	$946	$1,310	<$649>	<$285>
Percentage cost difference from CBT				<41%>	<18%>
Indirect costs to society					
Lost productivity during treatment	$3,729	$4,256	$3,781	$527	$53
Economic multiplier effect from lost productivity	8,017	9,150	8,130	1,133	113
Reduced taxes due to lost productivity	1,516	1,730	1,537	214	21
Lost income potential from suicide	1,913	1,913	1,913	0	0
Total costs to society	$15,174	$17,049	$15,362	$1,874	$187
Percentage cost difference from CBT				12%	1%
TOTAL TREATMENT COSTS	$23,120	$30,733	$31,245	$7,613	$8,125
Percentage cost difference from CBT				33%	35%

APPENDIX B
Data Used in Analysis

			Comments/Information sources
Patient/third party provider costs			
Health care provider and medication charges			
CBT:	# of regular sessions	15	from Wexler & Cicchitti
	Individual session charge	$100	UNR/VA rate
	Group session charge	$30	UNR/VA rate
	# of booster sessions	5	Assume charged at the individual session rate
Fluoxetine:	Retail cost per pill	$2.49	Safeway 6/7/96
	Pills per day	2	Greenberg et al., 1994
	# of physician sessions for prescriptions	16	Assume refilled every 45 days
	Average provider charges	$70	1/2 hr @ UNR Dept. of Psychiatry 6/27/96
Combination:	# of regular sessions	20	Assume psychiatric rate because prescription needed
	Average provider charges	$140	1 hour @ UNR Dept. of Psychiatry 6/27/96
Lost wages	Average net wage rate	$8.90	Assume $15/hr gross × (1 − tax rate in Community costs)
CBT:	Avg. time including travel per session	2.0	
	Individual sessions	2.0	hours
	Group sessions	3.0	hours
	Booster sessions	1.5	hours
Fluoxetine:	Time including travel per session	1.5	hours
Combination:	Time including travel per session	2.0	hours
Travel costs	Miles to doctor	10	Guess
	Miles to pharmacy	5	Guess
	Mileage rate	$0.30	IRS mileage allowance
Comorbidity	CBT	$1,030	per year from Simon et al.
	Fluoxetine and combination	$1,628	per year from Simon et al.
Costs to the community			
Economic multiplier effect from lost wages		2.15	times lost wages (source: BBER at UNR)
Reduced taxes due to lost wages		40.65%	FIT @ 28%, SIT @ 5%, FICA @ 7.65%
Reduced community service work by patients			
	CBT	$400	20 hours/year × $10/hour × 2 years
	Fluoxetine	$400	20 hours/year × $10/hour × 2 years
	Combination	$400	20 hours/year × $10/hour × 2 years
Costs to society			
Lost Productivity (242 workdays/year)			
	CBT	52	workdays lost (Greenberg et al., 1993)
	Fluoxetine	60	workdays lost (Greenberg et al., 1993)
	Combination	53	workdays lost (Greenberg et al., 1993)
Suicide		$1,913	workdays lost (Greenberg et al., 1993)

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