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Cost-Effectiveness of Bupropion, Nortriptyline and Psychological Intervention in Smoking Cessation

Abstract

Sustained-release bupropion and nortriptyline have been shown to be efficacious treatments for cigarette smoking. Psychological intervention is also recognized as efficacious. The cost and cost-effectiveness of the two drug therapies have not been estimated. It was hypothesized that nortriptyline would be more cost effective than bupropion. Hypotheses were not originally proposed concerning the cost-effectiveness of psychological versus drug treatment, but the two were compared using exploratory analyses. This was a 3 (bupropion versus nortriptyline versus placebo) by 2 (medical management alone versus medical management plus psychological intervention) randomized trial. Participants were 220 cigarette smokers. Outcome measures were cost and cost-effectiveness computed at week 52. Nortriptyline cost less than bupropion. Nortriptyline was more cost-effective than bupropion; the difference was not statistically significant. Psychological intervention cost less than the two drug treatments, and was more cost-effective, but not significantly so. Prospective investigations of the cost and cost-effectiveness of psychological and pharmacological intervention, using adequate sample sizes, are warranted.

Background and Significance

The current Clinical Practice Guidelines[1] endorse three treatments as efficacious for the treatment of tobacco dependence. One is the nicotine replacement therapies (NRTs) whose therapeutic mechanism is partial replacement of nicotine previously received through cigarettes, with the goal of tapering nicotine dose and achieving abstinence. The second is sustained release bupropion, originally marketed as an antidepressant. Its exact mechanisms of action are not known, but the drug has been shown to be efficacious for smoking cessation in multiple clinical trials[2, 3]. The third modality, psychological intervention, also has ample evidence for efficacy derived from well-designed experiments[1]. The Practice Guidelines also indicate that there are two drugs that should be considered as 'second-line' treatments for nicotine dependence. One of these is clonidine, an antihypertensive, and a second is nortriptyline, an older, tricyclic antidepressant[1-4]. These drugs are considered 'second-line' primarily because they have fewer studies supporting their efficacy.

The present study drew data from a clinical trial that compared the efficacy of bupropion, nortriptyline and psychological therapy. It was designed to estimate and test the relative cost-effectiveness of bupropion versus nortriptyline.

Psychological therapy is probably the most frequently used therapy in smoking cessation treatment provided by clinics, hospitals and other organizations. Bupropion is a prescription drug, and is often prescribed when smokers have tried NRT and failed. An informal survey of national health plans indicated that all these modalities are covered by most plans, but actual coverage depends on the benefits a particular employer chooses to offer.

Sustained release bupropion is a proprietary drug; nortriptyline is generic. The estimated cost per day of sustained release bupropion based on drug costs alone greatly exceeds that of

nortriptyline[5], so it might be expected that comparable efficacy would result in significantly higher cost-effectiveness for nortriptyline, despite the fact that nortriptyline may entail other costs. An example is blood draws to assess drug levels for dose adjustment. The study also included a psychological intervention. A comparison of the cost-effectiveness of psychological intervention to pharmaceutical interventions was not planned, however inspection of the data suggested that cost and cost-effectiveness comparisons might be of interest and hypothesis generating. Were nortriptyline to be found to be more cost-effective than bupropion, an argument could be made that it should be more widely prescribed than is now the case. Similarly, were the psychological intervention to be shown to be more efficacious, they might be more freely and frequently offered. It has long been assumed such interventions are expensive since they involve considerable staff time, and data to the contrary might increase their implementation. Thus, the present study evaluated two treatments that are considered first-line under current standards of care: bupropion and psychological treatment, and one second line treatment, nortriptyline. Were the hypotheses to be supported, we might expect a reappraisal of the relative rankings of these therapies, and perhaps a reconsideration of nortriptyline as a first-line therapy.

Hypotheses

The following hypotheses were proposed:

1. Cost of treatment: The cost of smoking cessation treatment per person treated using either bupropion or nortriptyline will be greater than medical management alone.
2. Cost-effectiveness: The cost-effectiveness of smoking cessation treatment using nortriptyline as an adjunct therapy to medical management is greater than that of bupropion as an adjunct to medical management.

In the exploratory analysis, psychological therapy was proposed to be more cost-effective than both nortriptyline and bupropion as an adjunct to medical management. As much as possible, we adhered to the Recommendations for Reporting Cost-Effectiveness Analyses proposed by the Panel on Cost-Effectiveness in Health and Medicine[6]. The Cost-Effectiveness Analysis completed in the present paper was from the perspective of the organization paying for health care—for example, a health maintenance organization, or a private insurer. The study took place from January 1997 through August 1999.

METHODS

A detailed description of the methodology and efficacy data for the study from which the data in the present study were obtained were reported elsewhere[3]. Briefly, this was a 2 (medical management versus psychological intervention) by 3 (bupropion versus nortriptyline versus placebo) randomized trial. Participants were 220 cigarette smokers. Outcome measures were biologically-verified abstinence from cigarettes at weeks 12, 24, 36 and 52. Treatment took place during weeks 1-12.

Using 7-day point-prevalence abstinence, both nortriptyline and bupropion were found to be more efficacious than placebo. The two drugs did not differ from each other or from placebo on one-year continuous abstinence. Psychological intervention produced higher 7-day point prevalence biochemically verified abstinence rates than medical management alone, and did not differ from either nortriptyline or bupropion in abstinence rates. Psychological intervention did not produce better continuous abstinence rates than medical management alone[3].

Participants

Participants were community volunteers recruited from the San Francisco Bay Area. All wanted to quit smoking and were willing to participate in a clinical trial to test the efficacy of

nortriptyline, bupropion and psychological intervention for smoking cessation. Interested individuals completed an informed consent and were invited to a baseline assessment including a physical examination and EKG. Even though blood levels were only needed for nortriptyline clinically, blood was drawn on all participants in order to maintain the blind. (See [3] for additional details.) Primary exclusionary criteria were those that would rule out use of either drug, plus health conditions that would interfere with the conduct of the study, including recent drug or alcohol abuse, use of other psychiatric medications, suicidal or psychotic symptoms, and use of other drugs for smoking cessation.

Assessments were at baseline and at weeks 12 (end of treatment), 24, 36, and 52. Participants were coded as non-smoking if they reported no cigarettes, not even a puff, during the previous 7 days; had expired carbon monoxide levels of 10 ppm or less; and urine cotinine levels of 60 mg/ml or less.

INTERVENTIONS

Medical Management

The medical management intervention was developed from the 1996 Agency for Health Care Policy and Research (AHCPR) Guidelines[7], the most recent version of the Practice Guidelines when the study was initiated. Because antidepressants were used, the medical-management condition used the guidelines of the pharmacotherapy condition of the Collaborative Depression Trials[8]. Medical management included advice on how to stop smoking, and on medication, side effects monitoring, and educational materials. It did not introduce complex or time-consuming interventions that would be impractical in a primary-care medical practice setting. Study physicians were five licensed psychiatric and internal medicine physicians and residents, who met briefly with participants at Weeks 1, 2, 6, and 11.

Pharmacological Interventions

Medication treatment was placebo controlled and double blind. All participants received capsules that were identical in number and appearance, independent of condition.

Participants met with a study physician at week 1 to begin medication treatment and weeks 2, 6, and 11 to review compliance and assess side effects. Nortriptyline drug dose was titrated for each participant until the therapeutic serum level for depression (50-150 mg/ml) was obtained. All participants assigned active nortriptyline received 25 mg/day for 3 days, followed by 50-mg/day for four days. At the end of this one-week period, serum levels of nortriptyline were assessed and dosage increased to 75 mg/day if a therapeutic serum level had not been reached. At week 4, serum levels were assessed again and, if necessary, drug dosage was increased to 100 mg. At week 6, serum levels were assessed to determine final nortriptyline dose.

Bupropion dose began at 150 mg/day for the first three days. The dosage was then increased to 300 mg/day from day 4 through week 12. Drug treatment was discontinued at the end of week 12 for both nortriptyline and bupropion.

Psychological Interventions

In addition to medical management, if participants were assigned to a condition including the psychological intervention, they participated in five group sessions. Providers were three masters level counselors, the modal smoking treatment provider in the health care organizations that were surveyed before the study was initiated. The group intervention was an adaptation of an intervention described in detail in the report of the clinical efficacy of the treatment[3], and a manual is available from the first author. It followed a behavioral model, integrated with cognitive techniques for mood management. Group size ranged from 3-11. The intervention

provided health-related information for mood management and smoking cessation, and discussion of cessation. Methods used included monitoring of cigarette use and affective states; paper and pencil exercises focusing on health-related information, motivation to quit, and decreasing relapse-related thoughts; informational handouts, and brief didactic presentations.

Cost-Effectiveness Methods

Definitions of Cost-Effectiveness Measures

The standard measure of cost-effectiveness is the incremental cost-effectiveness ratio (ICER), which is defined as

$$(C_{MM+Adjunct} - C_{MM})/(O_{MM+Adjunct} - O_{MM}).$$

The quantity $(C_{MM+Adjunct} - C_{MM})$, or incremental cost, is the difference between the expected cost of medical management (MM) with the adjunct (bupropion, nortriptyline, or psychological therapy), and the cost of the comparison treatment, MM alone. In this study, the quantity $(O_{MM+Adjunct} - O_{MM})$ is the incremental 52 week abstinence rate (outcome). The ICER provides a measure of the incremental cost per abstinent participant from adopting an adjunct treatment in addition to the comparison treatment.

The ICER is difficult to use in hypothesis tests. Equivalent analyses can be performed using the average cost-effectiveness ratio (ACER), which is more tractable for statistical hypothesis testing[9, 10]. Therefore, while the expected ICERs are reported for reference, the hypotheses tests were done using the ACERs of each treatment. The conclusions reached using the ACER as a cost-effectiveness measure also hold when using the ICER[9, 10].

The ACER is defined as C_T / O_T,

where C_T is the cost of treatment T,

and

O_T is the 52 week abstinence rate outcome.

The goal of cost-effectiveness analysis is to identify efficient treatments. An efficient treatment is one that is not both more costly and less effective a comparison treatment. In this study, abstinence from cigarettes at week 52 was the measure of efficacy. When comparing two or more treatments, as is appropriate for comparing MM alone and MM plus each adjunct, all treatments are ordered by increasing expected abstinence rates, and the treatment under consideration is tested for efficiency against the two adjacent treatments. Therefore, MM plus nortriptyline was tested against MM alone and MM plus bupropion (Figure 1).

The exploratory analysis of psychological intervention was conducted using the same method, which used the ICER to report expected cost-effectiveness and the ACER to conduct the hypothesis tests. Two pairwise tests were conducted: MM plus psychological intervention against MM alone and MM plus bupropion, and MM plus psychological intervention against MM alone and MM plus nortriptyline.

Statistical Methods

Costs

Overall differences between medical management alone, medical management + psychological intervention, medical management + nortriptyline and medical management + bupropion were tested using a one-way analysis of variance (ANOVA). Tests for differences between pairs of treatments used t-tests. To compensate for multiple comparisons, the significance level for each individual comparisons was adjusted from .05 to .008 using Bonferroni's method in which the original alpha level (.05) is divided by the number of comparisons (n=6) (0.05/6 = 0.008).

A second ANOVA was done to test determine whether there were differences between the psychological intervention, nortriptyline and bupropion when compared to medical management alone. Three pairwise comparisons were completed to identify distinct incremental costs of each adjunct over medical management alone, using a 0.05/3 -= 0.017 significance level for each test, for an overall significance level of 0.05.

Cost-Effectiveness and Efficiency

The efficiency of MM plus nortriptyline treatment was tested using the method described in Laska, Meisner and Siegal[9, 10]. In this method, each treatment is tested for efficiency in order of increasing observed efficiency. The method allowed a test of the efficiency of MM plus nortriptyline without assuming that MM alone or MM plus bupropion are efficient treatments. A weighted average ACER of MM alone and MM plus bupropion was constructed that had an outcome equal to that of MM plus nortriptyline. If the ACER of MM plus nortriptyline was found to be greater than the weighted average ACER, then MM plus nortriptyline would be considered inefficient in clinical practice. If the ACER of MM plus nortriptyline was found to be less than or equal to the weighted average ACER, MM plus nortriptyline would be considered efficient. A two sided test was performed, using the equality of the ACERs as the null hypothesis. The test statistic was the ratio of two ACERs: the weighted average ACER of the comparison treatments to the ACER of the intervention. The null hypothesis was that the ratio was 1.0, as described in Laska, Meisner and Siegal [9, 10]. The significance level of the two sided test was set at 5%.

The exploratory analysis for MM plus psychological therapy compared to the other treatments was done using the same method as for the drug treatments. Two pairwise tests were performed, one for MM plus psychological management against MM and MM plus nortriptyline, and against

MM and MM plus bupropion. Each test was done at a 5% significance level. In this case, the efficiency of psychological treatment was suggested after examination of the data. The exact significance level of the test is not of critical importance.

All analyses were done using SAS version 8.2.

Sensitivity Analysis

A "breakeven" sensitivity analysis was conducted to supplement the statistical analysis. Breakeven analysis allows visual determination of how much a selected parameter can change before a target therapy becomes inefficient relative to an alternative therapy. The observed ICER of the target therapy was plotted against a curve that represents all combinations of two selected variables that produce an ICER equal to that of the alternative therapy; and this curve is called the "breakeven curve." The farther the observed ICER for a therapy is from the breakeven curve, the less sensitive the results are to changes in the selected variables. A third variable was also altered where appropriate, holding the variable on the axes constant. This produced a shift in the breakeven curve. In this case, a new breakeven curve is created, and the breakeven value of the third variable was found by changing the observed value until the breakeven curve intersects the observed ICER.

Three breakeven analyses were performed. In the first, MM plus nortriptyline was compared to MM plus bupropion for all combinations of the effectiveness of MM plus nortriptyline therapy and the cost of proprietary bupropion. In the second, MM plus psychological intervention was compared to MM plus nortriptyline in terms of the effectiveness of MM plus psychological intervention and the price of nortriptyline. Finally, MM plus psychological intervention was compared to MM plus bupropion in terms of the effectiveness of MM plus psychological intervention and the price of bupropion.

Cost Data

The cost per abstinent patient was calculated for both active drugs from initiation of treatment to 52 weeks, from the perspective of a care provider or insurer who bears the direct costs of the intervention[11]. The expected treatment costs were obtained by valuing each participant's utilization of medication, physician's and other health professionals' time, and other treatment components at market prices and then averaging across participants within each treatment group. Average treatment costs and the prices used in their calculation are shown in Table 1. Hours of physician and counselor time expended in each participant's treatment were logged during treatment. Counselor hours were valued according to the salary and benefits of the masters-level counselors employed by the study. For this purpose, annual salaries and benefits were converted to hourly terms by assuming a 2000 hour work year (i.e., 40 hours per week for 50 weeks per year). Physician hours were valued in the same fashion except the compensation levels of the study physicians were not used; all were residents and thus had atypically low salaries. Physician time was valued using the median annual compensation reported by National Compensation Survey for physician practice income conducted in 2000, published in Monthly Labor Review (2002 12593).

The amounts of nortriptyline and bupropion distributed to each participant were recorded during treatment, and were valued at the lowest wholesale prices reported in the *Drug Topics Red Book*[12]. Since these prices apply to bulk pharmacy purchases, an estimate of dispensing costs was added based on the per-prescription dispensing charges allowed under the Medicaid program, which are reported in the *Red Book*[12]. Dispensing cost estimates assumed that participants received their medication in 30 day installments.

Nortriptyline medication costs include the costs of blood assays for titrating dosage. The study protocol included three assays for titration, which provided further empirical confirmation for the adequacy of the recommended adult dosage of 75-100mg/day[13, 14] for maintaining target plasma levels in the majority of participants. This number of blood assays is, however, atypical of clinical practice. Nortriptyline labeling only recommends blood assays for titration at dosages in excess of 100mg/day, and thus such assays are rare for most patients receiving nortriptyline in clinical settings[13, 14]. To make cost estimates more representative of clinical practice, only the costs of a single blood draw and assay for titration for each nortriptyline participant were included. Blood draws and assays are valued at the price charged by the San Francisco laboratory that performed the testing for the study subjects. Based on clinical practice, there was also an assumption that a baseline EKG would be required for all patients over age 50 and with a body-mass index greater than 30. The cost of each EKG was $38.

Two additional components of the treatment costs were the rental value of the office space used for physician visits and group counseling sessions, and the cost of written smoking cessation materials. Estimated space costs were based on the monthly rent per square foot of the San Francisco office that served as the study treatment site. Written materials were valued at either the publisher's price or the cost of duplication. With the exception of the medication prices, which are from current year compendiums, all prices were adjusted for inflation to mid-year 2000 terms using the Consumer Price Index.

The cost estimates excluded indirect costs borne by the treated smokers (for example, earnings forgone due to missed work hours), and expenditures undertaken for research purposes that would not be typical in a clinical implementation (for example, data collection costs and blood samples taken from participants to maintain the blind).

RESULTS

Participants

Due to a medical emergency, it was necessary to break the blind for one participant. That participant, who was on placebo drug, was discontinued from the study. Thus, the usable sample (N=219) was men (n=122) and women (n= 97), 18 years or older, who smoked 10 or more cigarettes per day and wanted to quit smoking. Comparisons of the six treatment cells indicated no significant differences among conditions on demographic or smoking related variables. Analyses and a table showing summary statistics for each condition are in [3], page 932.

Attrition

At the 52 week assessment follow-up data collection was completed on 81% (n=177) of the sample. There were no significant differences between drugs or psychological treatment on number of assessments missed.

Cost and Cost-Effectiveness

Estimated Costs and Cost-Effectiveness

The estimated cost of treating one smoker, abstinence rate, ICER and ACER are reported in Table 2. The treatments ranked in order of increasing abstinence rate were MM alone, MM plus psychological intervention, MM plus nortriptyline, and MM plus bupropion. The point estimates of the cost per treatment were $40, $75, $117 and $277 for MM alone, MM plus psychological intervention, MM plus nortriptyline, and MM plus bupropion, respectively. The ACERs were $313, $360, $504, $978, respectively. The ICERs of MM plus each adjunct treatment, compared to MM, were $440, $741, and $1,509 for MM plus psychological intervention, MM plus nortriptyline and MM plus bupropion, respectively (See Figure 1 and Table 2).

Cost of bupropion versus nortriptyline

The ANOVA indicated significant differences among the four treatments. The t-tests found that the mean costs of all four treatments differed at an overall significance level of 5%. Similarly, the second ANOVA indicated significant differences among the incremental costs the adjunctive therapies. Subsequent t-tests indicate that the differences in the three incremental costs were statistically significant

Hypothesis test of efficiency of nortriptyline

The ratio of the ACER of medical management plus nortriptyline treatment to the weighted average ACER of MM and MM plus bupropion was 0.68 (0.95% CI: 0.32, 2.32). It will be noted that the confidence interval (CI) of the Odds Ratio (OR) crosses 1.0.

Thus, no significant difference in cost-effectiveness between treatments was observed.

Exploratory Analysis of Efficiency of Psychological Treatment

The ratio of the ACER of psychological treatment to the ACER of the weighted average ACER of MM and MM plus nortriptyline was 0.77 (0.95% CI: 0.30, 2.87). The ratio of the ACER of psychological treatment to the equivalent combination of medical management and bupropion treatment was 0.55 (0.95% CI: 0.21, 1.61). Again, the CI crosses 1.0; therefore the differences are not statistically significant.

Sensitivity Analyses

The breakeven analysis of MM plus bupropion and MM plus nortriptyline treatments are shown in Figure 2. Holding the value of all other variables constant, MM plus nortriptyline would be more cost effective until bupropion cost less than $0.75 per 150 mg, and until the efficiency of nortriptyline was less than 0.20. Holding constant the observed effectiveness of nortriptyline and bupropion, and holding the current price of bupropion constant, nortriptyline

would be more cost-effective until the effectiveness of bupropion exceeded 0.44. The price of bupropion would have to fall by 50% in order for it to be more cost effective than MM plus nortriptyline.

The breakeven analysis for MM plus nortriptyline and MM plus psychological intervention is shown in Figure 3. MM plus psychological management is more cost-effective than MM plus nortriptyline for any positive cost per mg of nortriptyline. It is also more cost-effective until the efficiency of psychological intervention is less than 0.18. MM plus psychological intervention is more cost-effective until the effectiveness of nortriptyline exceeds 0.34.

The breakeven analysis for MM plus psychological intervention compared with MM plus bupropion is shown in Figure 4. MM plus psychological intervention is more cost-effective until the cost of bupropion was lower than $0.38 per 150 mg, or until the efficiency of psychological intervention was lower than 0.16. Holding constant the observed cost of bupropion and efficiency of psychological intervention, psychological intervention would be more cost-effective until the effectiveness of bupropion exceeds 0.72.

DISCUSSION

The statistical tests failed to find significant differences between treatments. Post-hoc power analyses indicated that the power of all tests was only between 10% and 50%. Estimations were made that, in order to show significant differences between bupropion and nortriptyline, 131 subjects per condition would be needed; while to show significant differences between nortriptyline and psychological treatment, 415 subjects would be needed; and 65 subjects would be needed to attain this level of power in the comparison between bupropion and psychological treatment using a 0.05 significance level for a test with a power of 0.80. These

sizes are larger than those in the present study, but they are within the range of those seen in clinical trials.

The magnitude of the effects can be seen by considering the magnitude of the costs that would be incurred to obtain equivalent effectiveness. For example, using the ACER, the findings of the present study imply that a combination of the two comparison treatments (MM alone and MM plus bupropion) that was equal in efficiency to MM plus nortriptyline alone with be 47% more costly per one-year quit than MM plus nortriptyline alone. Using the ICER to estimate, the data suggest that an equivalent combination of MM alone and MM plus bupropion would be 85% more expensive per one-year quitter than MM plus nortriptyline. This implies an effect of substantial practice significance. Similarly, the data imply that a combination of the two comparison treatments (MM alone and MM plus nortriptyline) that was equivalent in effectiveness to MM plus psychological treatment would be 30% more costly per one year quitter than MM plus psychological treatment were the ACER to be used, and 65% more expensive were the ICER to be used. Also, using the ACER, an equivalent combination of the two comparison treatments (MM alone and MM plus bupropion) would be 81% more costly per one-year quit than the treatment of MM plus psychological treatment alone. Using the ICER, the cost is 108% greater. Again, the comparisons imply effects of meaningful clinical significance.

A limitation of the present study is that it was based on outcome data derived from a clinical trial. While this method has advantages, including precise specification of treatment-related costs that are collected as the intervention is conducted, it is widely acknowledged that clinical trial participants may differ from the general population, and thus the results may not be widely generalizable. On the other hand, clinical practice relies on efficacy data collected in such trials.

It can be argued that the comparison between nortriptyline and bupropion is not very meaningful, because of the greater exclusions due to nortriptyline. Nortriptyline has been shown to be related to an increased rate of serious cardiac events in patients with ischemic heart disease. However, nortriptyline is cheaper than sustained release bupropion, and where it can be safely used, it provides an alternative treatment that is almost as efficacious and with comparable cost-effectiveness to bupropion.

The results for psychological intervention are very similar to those for nortriptyline and they seem noteworthy. It has long been assumed that psychological treatments are expensive. They are not, and given an appropriate experimental design, it is likely that cost-effectiveness for them over pharmacological treatment would be demonstrated. Perhaps less surprising, but also of interest, is the finding that the cost effectiveness of bupropion would have to fall 50% to equal the cost effectiveness of nortriptyline.

Clinical considerations, cost, and patient preference will often determine the choice of treatment, and those considerations may eliminate any one of the three adjunctive therapies considered here for a given smoker. Therefore the finding that all three therapies are cost-effective is important. Each should be made available to smokers, and this availability will be particularly important if other therapies cannot be used. Other considerations might also dictate choice of therapy. The costs from the patients' perspective were not included in these analyses, and would differ by type of therapy. They would be highest for the psychological intervention, because of the group attendance, and lowest for bupropion. Nortriptyline would fall in between the two, because additional time would be required of the patient to obtain blood samples and EKGs. Similarly, some providers might hesitate to use nortriptyline because of the extra monitoring involved in nortriptyline usage. However, others might find the availability of

therapeutic blood levels reassuring. It has long been argued that patients in the United States are more likely to accept drug therapies as opposed to psychological interventions. While we are unaware of data to support this claim, we have no reason to doubt it, and this preference certainly will enter into determining the treatment provided. The quit rate for bupropion in the clinical trial was higher than nortriptyline, though not significantly so. Willingness to pay for increased efficacy by an insurer is no doubt linked to the size of the difference between treatments, as well as the costs of treating tobacco related diseases. Given that these are considerable, increased efficacy may well justify increased cost. An example is in a recently published paper, where it was found that year long provision of pharmacotherapy and psychotherapy resulted in a 50% abstinence rate at one year, about twice that usually observed[4]. Even though the costs of such an intervention are clearly higher than those involved in traditional (brief) treatment the marked increase in efficacy might well result in willingness to pay on the part of insurers.

Implications for Behavioral Health Services

The first implication of these findings for behavioral health services is the need for additional cost-effectiveness analyses of bupropion and nortriptyline for the treatment of cigarette smoking, using adequate sample size. Currently, given lack of a significant difference between the two drugs in a health care setting, choice of drug will depend on patient characteristics, including exclusionary criteria and treatment history. Of greater interest, perhaps, is the relationship of psychological intervention to drug therapy. It has long been assumed that psychological intervention is expensive and not cost-effective. These data do not support that assumption, and suggest that in fact, in the appropriate experimental design, psychological intervention might exceed drug therapy in cost effectiveness. Even these preliminary findings do suggest however, for service providers, that psychological intervention

certainly should not be eliminated due to anticipated high costs, because there is no suggestion of that in their data. The psychological intervention used in the present study was on the higher end of the continuum of number of sessions provided. It may be that fewer sessions would be about as efficacious, but less costly, thus increasing the cost-effectiveness further. However, since the efficacy of psychological interventions is related to their intensity, this question will only be addressed by additional research.

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Figure 1. Incremental Cost Effectiveness of nortriptyline and bupropion versus medical management (Note MM+Placebo is the reference treatment, located at the origin)

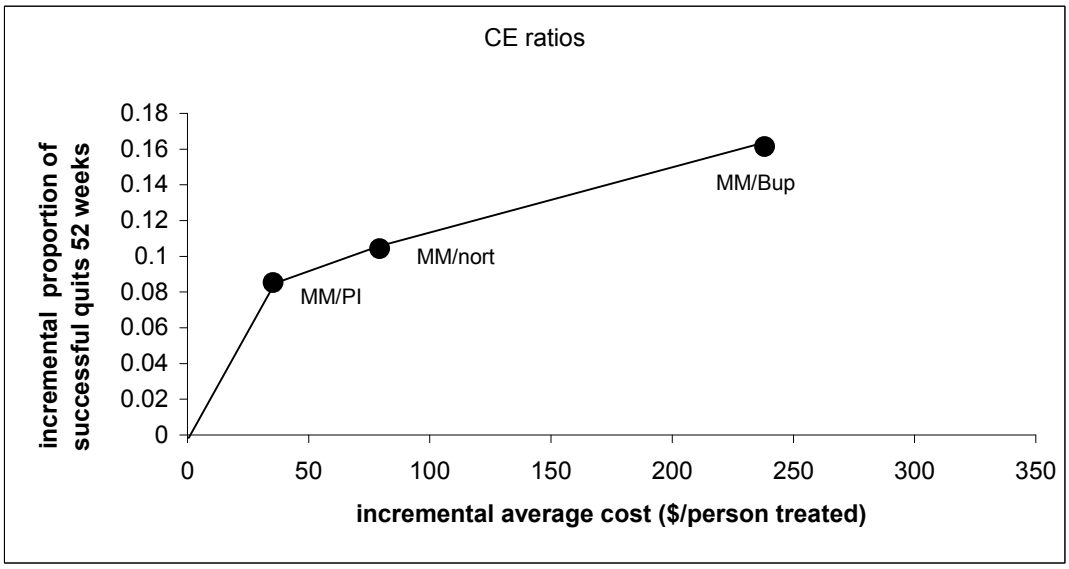

Figure 2. Breakeven analysis of the cost-effectiveness of nortriptyline versus bupropion.

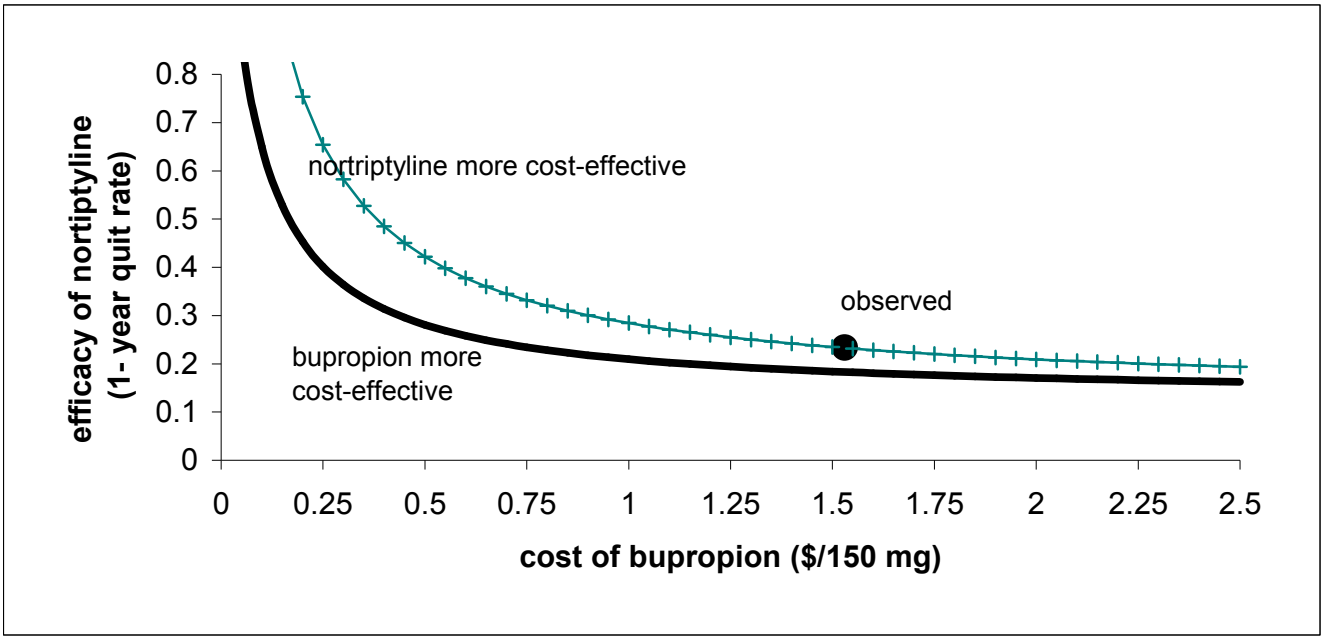

Figure 3. Breakeven analysis of psychological counseling versus nortriptyline.

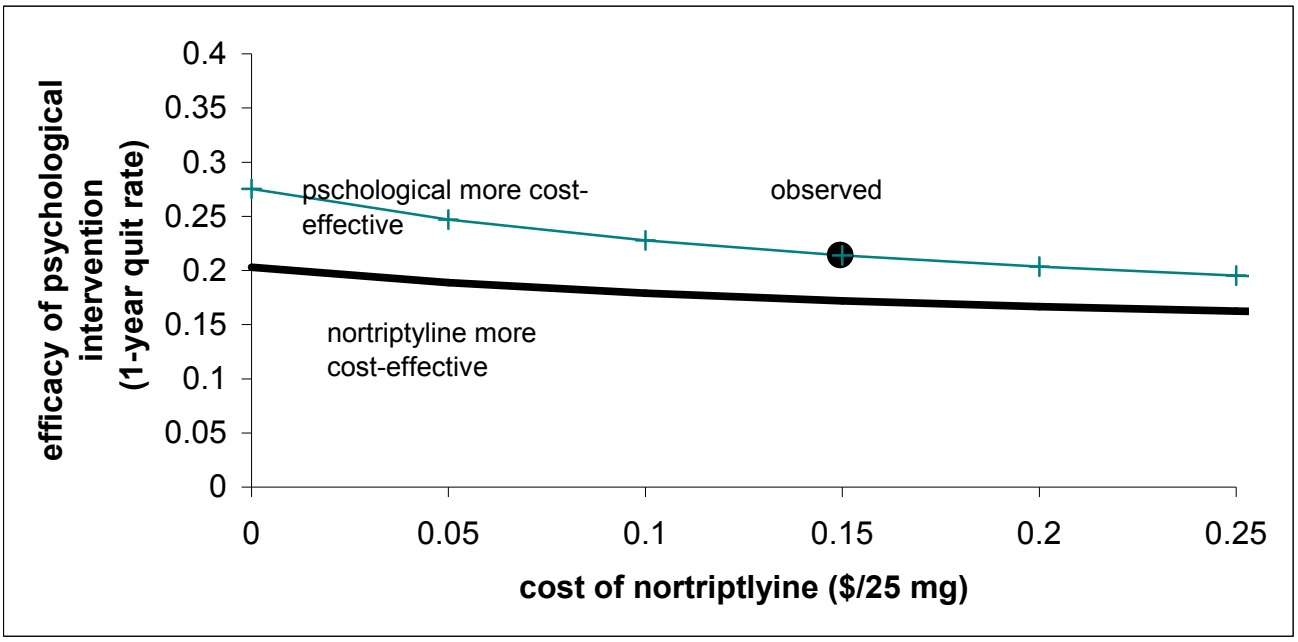

Figure 4. Breakeven analysis of psychological counseling versus bupropion.

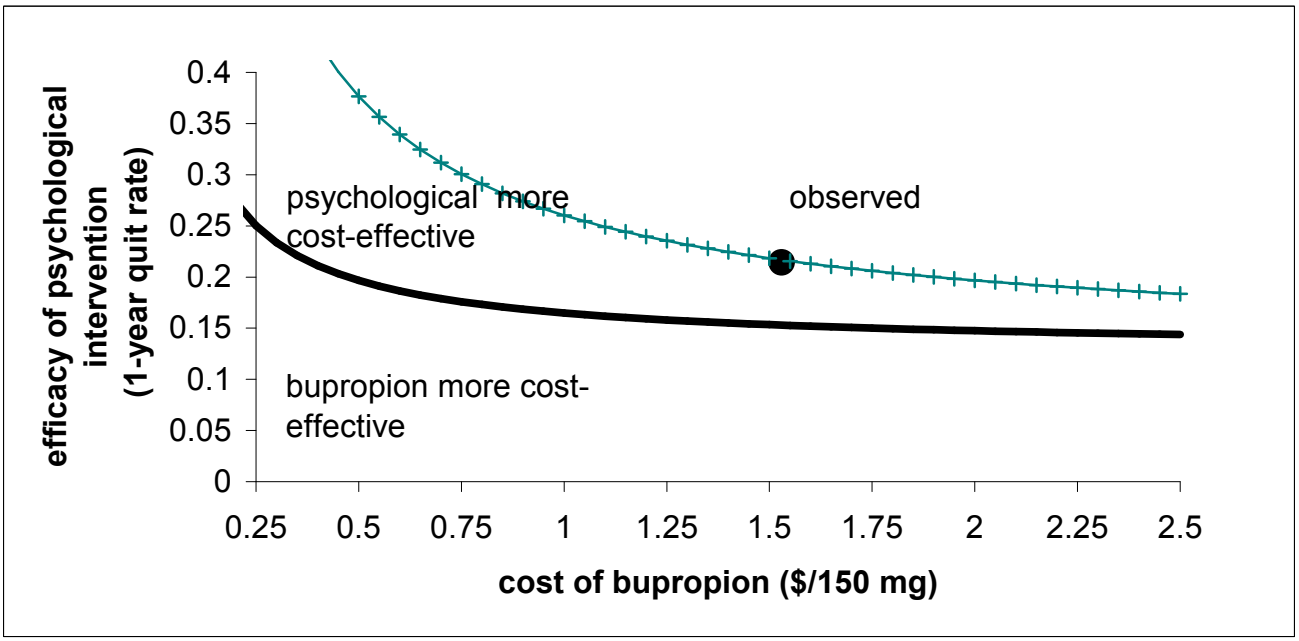

Table 1
Summary of Treatment Costs

cost component	Price	Placebo + MM	Placebo + MM/PI	Nortrip + MM	Bup + MM
Bup 150 mm SR	$1.53/tab	0.00	0.00	0.00	237.41
Nortrip 25 mg	$0.1495/capsule	0.00	0.00	43.80	0.00
Blood Draw/Assay	$21/draw+assay	0.00	0.00	21.17	0.00
Physician Time	$61/hour	30.60	29.76	34.11	31.40
Counselor Time	$16/hr	0.00	25.50	0.00	0.00
Space Rental	$0.007/sqft/hr	0.27	1.59	0.32	0.28
Written Materials	$8 MM, $11 PI	8.36	17.70	8.36	8.35
EKG cost	$38/test	0	0	10.89	0
Total Average Cost		**39.23**	**74.55**	**118.65**	**277.44**

Table 2
Cost and incremental cost-effectiveness of smoking cessation treatments (bootstrap estimates)

Treatment	Subjects	Cost per person treated			Percent Abstinent at 52 weeks	Mean ICER**	ACER***
		$\bar{x}$	SD	SE			
MM	37	$40	31	$5	0.13	--	$313
MM/PI	36	$75	47	$8	0.21	$440	$360
Nortrip + MM	38	$119	25	$4	0.23	$741	$504
Bup + MM	36	$277	90	$15	0.29	$1,509	$978

*ICER: Incremental Cost Effectiveness Ratio
**Efficacy: the proportion of quitters at 52 weeks
***ACER: Average Cost Effectiveness Ratio