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Cost-Benefit Analysis of Sustained-Release Bupropion, Nicotine Patch, or Both for Smoking Cessation[1]

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Background. **The nicotine transdermal patch (NTP) has been shown previously to be a cost-effective smoking cessation intervention. This is the first economic analysis comparing the NTP with the only non-nicotine-containing pharmacological intervention, bupropion HCl.**

Methods. **Decision-tree analysis, based on a previously published cost-benefit smoking-cessation model, was used to determine the optimal treatment from the standpoint of costs versus benefits, from the employer's perspective. Base-case probabilities of successful quitting in our model came from clinical trial point-prevalence data at the end of a 1-year follow-up study (N = 893) comparing placebo, bupropion, NTP, and bupropion/NTP in combination, administered along with minimal counseling. Sensitivity analyses were performed to determine the effects of variations in base-case assumptions regarding the monetary benefits that would accrue if an intervention were successful, probabilities of quitting, drug costs, cost of lost work time for a health care provider visit, and cost of the visit itself.**

Results. **The analysis showed that bupropion is more cost-beneficial than either NTP or bupropion/NTP, with a net benefit in the first post-quit year of up to $338 per employee who attempts to quit compared with $26 for NTP, $178 for the two in combination, and $258 for placebo. These results were robust to most plausible variations in the assumptions used in the model. One exception was the monetary benefit of successful intervention (assumed in the base-case to be $1,654). If this benefit were actually less than $1,112, placebo (i.e., minimal counseling with no pharmacological intervention) would be more cost-beneficial than any of the active treatments.**

Conclusion. **From an employer's perspective, bupropion 300 mg/day for 9 weeks is a more cost-beneficial smoking cessation intervention than the nicotine patch, and under most scenarios, bupropion is also more cost-beneficial than placebo.**

Key Words: **smoking cessation; bupropion; nicotine transdermal patch; cost-benefit; economic analysis.**

INTRODUCTION

As the leading preventable cause of death in the United States, smoking is one of the greatest public health and economic concerns facing the United States [*1*]. Medical care costs and lost wages due to smoking-related morbidity and mortality amount to an estimated $100 billion annually in the United States [2]. Costs to employers alone have been estimated to be as high as $10,000 per smoker yearly (in 1997 dollars), based on the cost of medical care, absenteeism, accidents, and lost work time associated with smoking-related illness [*3–5*].

Whereas treatment programs to help smokers quit will also cost money, these costs may be offset through savings resulting from reductions in smoking-related illness [*6,7*] and incremental costs per life-year saved [*8,9*]. Assuming that employers would bear the largest portion of the expense for a smoking cessation program through employee health initiatives or insurance, we conducted an economic analysis from the employer's perspective of the cost and savings that could be expected by funding employee smoking cessation efforts. The analysis used a cost-benefit model, which attempts to predict the net benefit to a payer in monetary terms based on the gross benefits and costs given certain scenarios or assumptions.

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The cost-benefit model presented here is based on the earlier work by McGhan and Smith [5], who developed a model of the economic cost and benefit associated with seven different smoking interventions: self-help, nicotine patches, behavioral treatments (group and individual counseling), and combinations of behavioral treatments and the nicotine patch. Costs, quit rates, and expected benefits were taken from meta-analyses and a national survey of nicotine patch users who received a smoking-cessation consultation from a pharmacist. The potential benefit to employers for each smoker who quit was assumed to be $1,483 (in 1994 dollars) in the first year. This figure represented savings from reduced absenteeism, medical care and workers' compensation costs, and lost productivity. The authors concluded that a smoking cessation program consisting of treatment with nicotine patches, consultations with pharmacists, and participation in a comprehensive behavioral program would be the most cost-beneficial to employers, at $302 (in 1994 dollars) per smoker who attempts to quit in the first year. In our model, we use the same potential benefit (savings) per successful quitter in the base-case scenario along with quit rate data from a clinical efficacy trial comparing placebo, a nicotine transdermal patch (NTP), bupropion, and a combination of NTP and bupropion.

METHODS

Cost-Benefit Model

The model reflects the costs, probabilities (quit rates), and benefits associated with a clinical efficacy trial evaluating four smoking-cessation regimens. The detailed methods for this clinical efficacy trial have been published elsewhere [10]. Briefly, the study was a double-blind, placebo-controlled comparison of sustained-release bupropion (Zyban) (244 subjects), an NTP (Habitrol Nicotine Transdermal System) (244 subjects), bupropion and NTP (245 subjects), and placebo (160 subjects). Treatment consisted of 9 weeks of bupropion (150 mg a day for the first 3 days and then 150 mg twice daily) or placebo, as well as 8 weeks of NTP (21 mg per day during weeks 2 through 7, 14 mg per day during week 8, and 7 mg per day during week 9) or placebo. The primary outcome variable was the point-prevalence rate of abstinence at 6 and 12 months of follow-up. Subjects were considered abstinent if they reported not smoking since the preceding clinic visit and had an expired carbon monoxide concentration of 10 ppm or less at all clinic visits during the 12-month study. Baseline characteristics of the subjects at baseline were similar (Table 1).

Figure 1 displays the decision-tree analysis. To the right of the "randomization" node are four branches, each representing a treatment arm from the trial. To the right of each of these is a pair of branches representing the two possible outcomes: the patient quits smoking ("Quit") or the patient relapses and continues to smoke ("Smoke"). On each Quit branch is the probability of quitting (P_Q) for that treatment arm; under each Smoke branch is the probability of resuming smoking ($1 - P_Q$) for that treatment arm. The terminal nodes to the far right represent the net benefit for each possible outcome, with "QuitSavings" representing the possible savings to the employer for each successful quitter, "CostTx" representing the cost of the treatment, and "SmokeSavings" representing no savings (i.e., $0). The decision analysis was programmed in DATA 3.0 [11].

Costs

Drug costs were based on the average whole price (AWP) for bupropion and the NTP [12], administered per labeling. Using the clinical trial dosing schedule, the cost of bupropion was $163.49 for a full course (300 mg/day at $2.66 per day for 60 days plus 150 mg/day at $1.33 per day for 3 days). The cost of the NTP was $245.24 for a full course (21-mg patches at $4.46 per day for 42 days, 14-mg patches at $4.24 per day for 7 days, and 7-mg patches at $4.02 per day for 7 days).

Probabilities

Quit rates, reflected in the decision tree (Fig. 1) as the probability of successful quitting, were point-prevalence quit rates at 1 year (rates of abstinence during week 52). Quit rates were 15.6, 16.4, 30.3, and 35.5%, for patients receiving placebo, NTP, bupropion, or bupropion/NTP, respectively.

Benefits

In the base-case scenario, we assumed a benefit to employers of $1,483 (1994 dollars) per successful quitter in the first year (based on the model of McGhan and Smith [5]). We adjusted this figure to 1998 dollars using the consumer price index general inflation rate through 1997 [13] plus an estimate of 3% for 1998, yielding an inflation-adjusted figure of $1,654. Net benefit for each treatment arm was calculated by multiplying the quit rate (P_Q) by the benefit associated with quitting (QuitSavings minus CostTx) and adding to that the product of the relapse rate ($1 - P_Q$) and the (negative) net benefit of continuing to smoke (QuitSavings of 0 minus CostTx).

Sensitivity Analyses

Several one-way sensitivity analyses (i.e., only one assumption was manipulated at a time, with all others remaining constant) were conducted to assess whether the outcomes from the model would be likely to differ under plausible variations in the base-case assumptions (Table 2). The drug costs were varied from the

TABLE 1

Baseline Characteristics of Subjects[a]

Characteristic	Placebo (n = 160)	Bupropion (n = 244)	NTP (n = 244)	Bupropion/NTP (n = 245)
Age(yr)	42.7	42.3	44.0	43.9
Sex (% female)	58.8	51.6	51.6	49.4
Ethnic origin (% white)	93.1	93.0	93.9	92.2
No. of cigarettes smoked daily	28.1	25.5	26.5	26.8
No. of previous attempts to quit	2.8	3.1	2.7	2.5

[a] Mean values are shown, except for sex and ethnic origin.

AWP by ±25% (rounded to the nearest dollar). Probabilities of quitting were varied from the lower to the upper bound of the 95% confidence interval around the point-prevalence quit rate (i.e., from the lowest probable estimate to the highest probable estimate based on an α of 0.05). Although the base-case scenario does not consider the costs of lost time from work to visit a health care provider or the cost of the health care provider visit, these costs were also subjected to sensitivity analysis. Because patients in the placebo arm received the same brief counseling as those receiving the active treatments, cost of a health care provider visit was varied in all arms, rather than just in the active treatment arms. Cost of lost work time for a health care provider visit was varied from \$0 to \$50 (\$50 being twice the expected cost of 2 missed hours at \$12.50/h, which is just over the median hourly wage across all jobs nationally in 1997 according to the Bureau of Labor Statistics figures). Cost of a health care provider visit was varied from \$0 to \$75. The cost-benefit to the employer was varied from \$0 to the base-case assumption of \$1,654.

Adjustments and Discounting

Costs and benefits were adjusted when necessary in order to be expressed in 1998 dollars. Expected benefits were not discounted, because the time horizon of the analysis was only 1 year.

RESULTS

Base-Case Cost-Benefit Analysis

The results of the cost-benefit analysis, using the base-case assumptions, are illustrated in Fig. 2. The model shows that bupropion is more cost-beneficial than NTP alone or than both used in combination, with

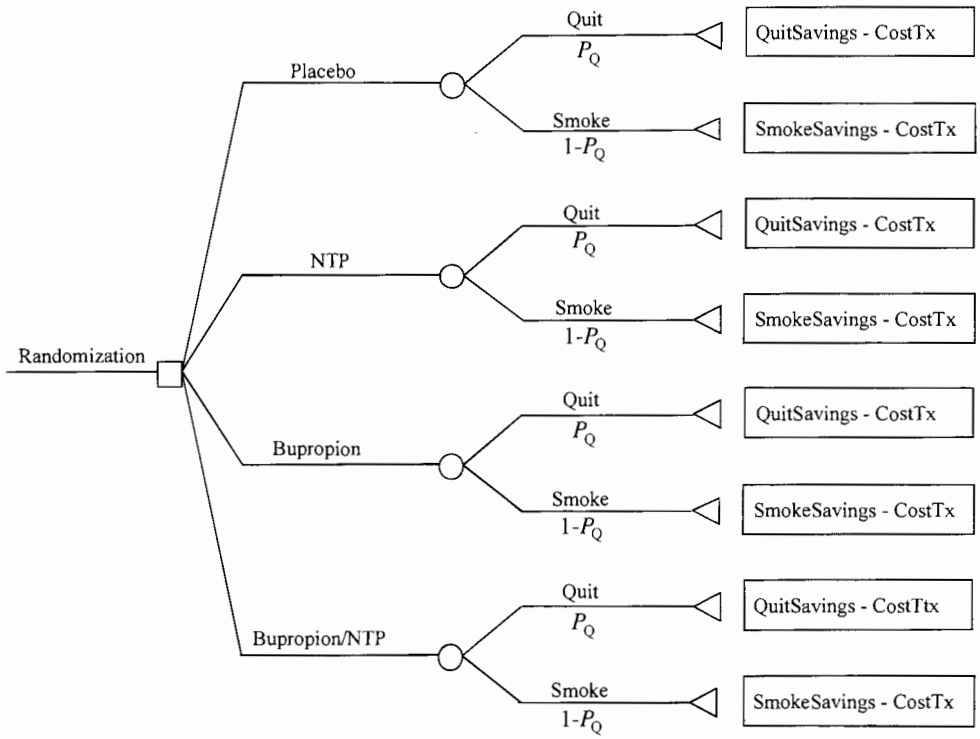

FIG. 1. Decision-tree analysis.

TABLE 2

Base-Case Assumption and Ranges Used in Sensitivity Analyses

Assumption (range)	Placebo	Bupropion	NTP	Bupropion/NTP
Drug costs	$0	$163.49	$245.22	$408.71
(±25%)	n/a	($122.62–204.36)	($183.92–306.53)	($306.54–510.89)
Probabilities	0.156	0.303	0.164	0.355
(95% confidence interval)	(0.104–0.222)	(0.246–0.365)	(0.120–0.216)	(0.295–0.419)
Benefit per successful quit		$1,654 ($0–1654)		
Cost of work time lost for health care provider visit		0($0–50)		
Cost of health care provider visit		0($0–75)		

Note. Costs are expressed in 1998 dollars. n/a, not applicable.

a net benefit in the first post-quit year of up to $338 per employee who attempts to quit compared with $26 for NTP, $178 for the two in combination, and $258 for placebo. Although the bupropion/NTP treatment arm had a better quit rate than bupropion alone (0.355 vs 0.303, respectively), the difference was not statistically significant ($P = 0.271$) and it did not outweigh the difference in drug costs used in the model.

Sensitivity Analysis

The model was sensitive to changes in some assumptions regarding quit rates (probabilities). Substituting quit rates at the top and bottom of the 95% confidence interval around each point prevalence rate had an effect only when bupropion and placebo were compared. If the true value of the quit rate for the placebo arm were, in fact, above 20.4% (with bupropion held constant), then placebo would be more cost-beneficial. Similarly, with placebo rates held constant, if the true value of the quit rate for the bupropion arm were less than 25.5%, then placebo would also be the more cost-beneficial option. These analyses are shown in Figs. 3 and 4.

The model was not sensitive to variation in the drug costs within the range of the AWP ±25%. The results were also robust with respect to the cost of lost work time for a health care provider visit (up to $50) and to the cost of the visit itself (up to $75).

The model was sensitive to variations in assumptions

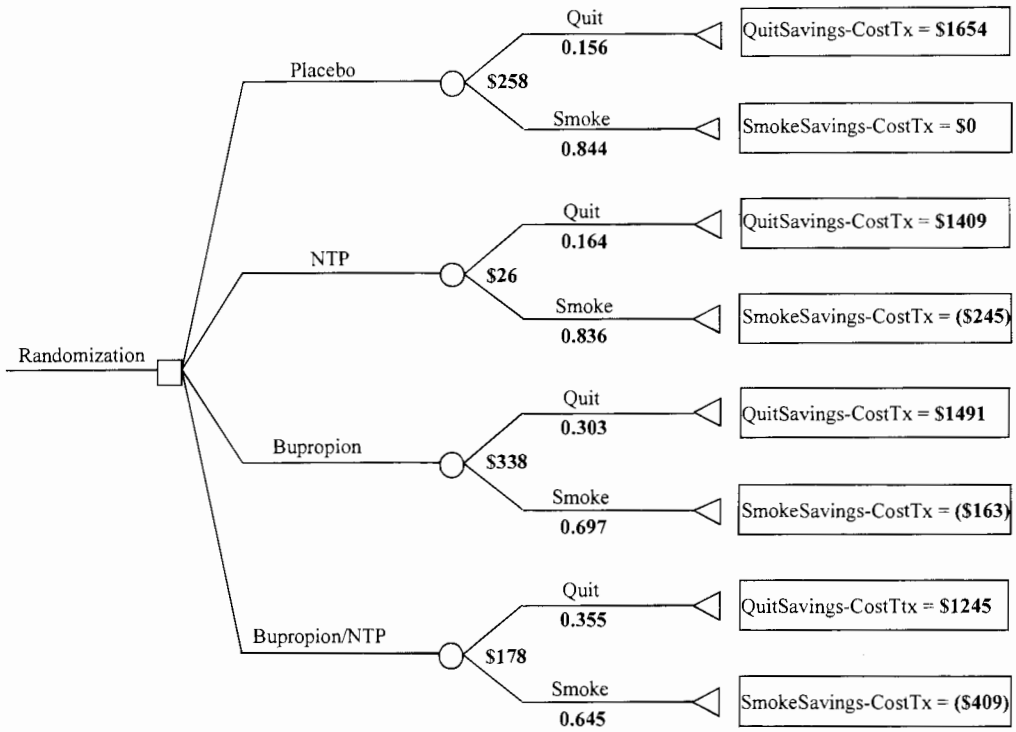

FIG. 2. Outcome of the cost-benefit analysis. Cost-benefit is derived as follows: P(quit), × (QuitSavings − CostTx) + P(smoke), × (QuitSavings − CostTx) = net benefit. For the NTP arm, this calculation (to the nearest whole dollar) would be [0.164, × (1,654 − 245)] + [0.836, × (0 − 245)] = $26.

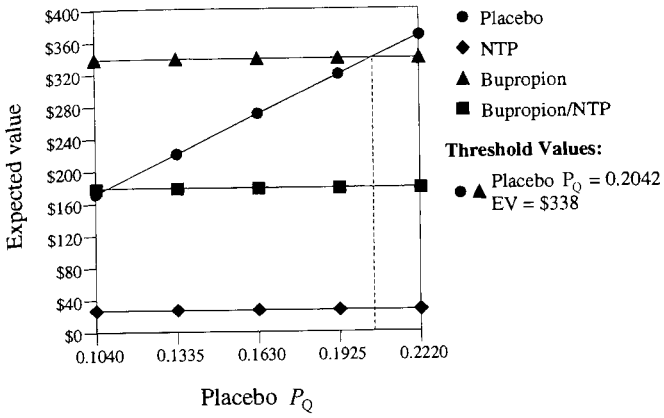

FIG. 3. Sensitivity analysis on quit rate for placebo.

regarding the monetary benefit of successful intervention (QuitSavings). As shown in Fig. 5, the threshold value, i.e., the amount below which no net benefit would be realized, was $1,112. If the benefit were less than that amount, placebo would be more cost-beneficial than any of the active treatment arms, in that the drug costs combined with the probabilities of success would yield net benefits to the employer lower than that for placebo (i.e., $258).

DISCUSSION

Cost-benefit analysis is an economic analysis technique that takes into account the effectiveness of an intervention, the cost of the intervention, the cost of failure of that intervention, and the monetary benefits that would be realized if the intervention were successful. The present cost-benefit analysis was from the perspective of the employer, who might, for example, reimburse the employee for smoking-cessation treatment through experience-rated or self-insured health insurance plans, direct reimbursement for prescription costs, or work-site health promotion efforts. The employer would thus bear the costs of treatment for each quit attempt, regardless of whether the employee was ultimately successful in quitting. However, the benefits accruing to the employer from reductions in absenteeism, accidents, and health care costs, as well as from avoiding reduced work productivity resulting directly from the smoking ritual (approximately 40% in one survey reported leaving work to smoke one or more times per day during non-break periods [*14*]), would apply only for successful quitters. Thus the cost-benefit analysis provides a net benefit in which treatment costs are subtracted from success-rate-weighted benefits for each treatment arm.

In this analysis, the treatment conditions were self-help with minimal counseling, combined with placebo, bupropion, NTP, or the combination of bupropion and NTP pharmacotherapy. The net benefit for the bupropion arm was $338 compared with $258 for placebo (minimal counseling without pharmacotherapy), $178 for bupropion/NTP, and $26 for NTP. Based on this model, it is clear that any of the smoking cessation interventions provides at least a small net benefit, but bupropion is the most cost-beneficial aid in smoking cessation.

Sensitivity analyses were conducted to test the assumptions of the model. Any economic model must contain assumptions, and sensitivity analysis is a method for testing whether variations in the assumptions would change the outcome of the analysis. (Ideally, a model will be robust to plausible variations; if not, the conclusions are less easily supported.) The model was insensitive to cost variations of AWP ± 25%, a generous range to allow for price variations. In addition, neither the cost of lost work time associated with a health care provider visit nor the cost of the visit itself altered the conclusions. Thus, none of the basic cost assumptions threatens the validity of the model.

When the quit rates were varied within the range of the 95% confidence intervals of probabilities for each treatment arm, the model was robust to most variations, with the exception of the upper and lower bounds

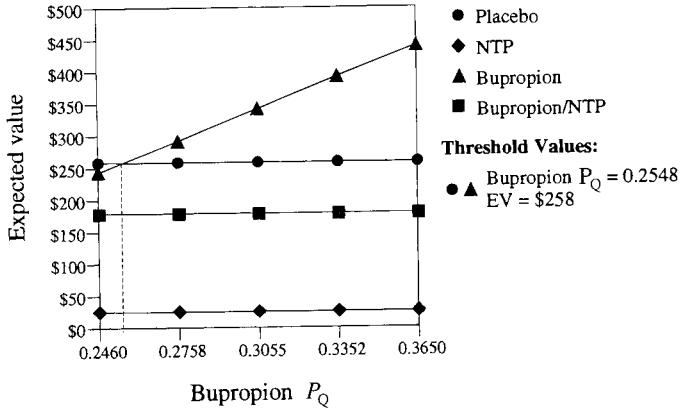

FIG. 4. Sensitivity analysis on quit rate for bupropion.

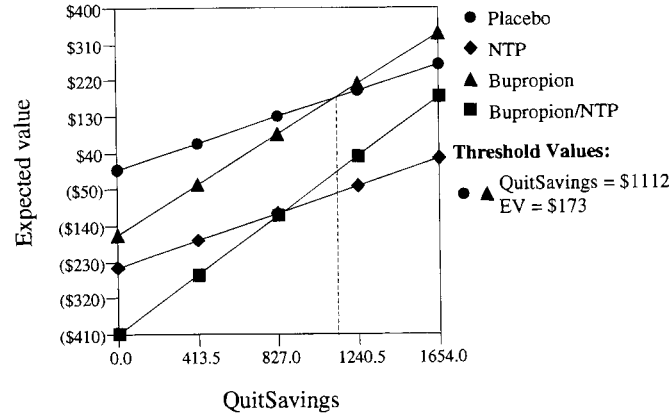

FIG. 5. Sensitivity analysis on the potential savings to the employer for each successful quitter (QuitSavings).

of the 95% confidence interval around placebo and bupropion quit rates. In order for placebo to be more cost-beneficial than bupropion, the placebo quit rate would have to exceed 20.4% or the bupropion quit rate would have to be lower than 25.5% (in either scenario, holding the other quit rate constant). Published quit rates for minimal or brief counseling range from approximately 9 to 12% [*9*], so it seems improbable that this trial's higher-than-average placebo quit rate has been underestimated. Sufficient data do not exist to evaluate the likelihood that the true 1-year quit rate for bupropion actually falls below 25.5%.

The model was sensitive to assumed benefit to the employer for a smoker who quits. The figure used was derived by inflating McGhan and Smith's figure of $1,483 (1994 dollars) [*5*] to 1998 dollars. The figure used by McGhan and Smith was the most conservative that they could find in the literature. In fact, the original paper from which it was derived [*15*] also sought to use the most conservative possible figures, often cutting the estimates arbitrarily in half in order to ensure that over-estimation was avoided. Given these conservative approaches, the benefit estimate seemed reasonable at face value. Nevertheless, the sensitivity analysis demonstrated that if the actual benefit per successful quitter were $1,112 or less, then placebo would be the most cost-beneficial option (under the conservative assumption that non-pharmacological treatment incurs no cost). If one lacked confidence in the McGhan and Smith figure, the sensitivity of the model to this estimate would be problematic. However, other data suggest that the $1,654 figure is defensible.

Bertera in 1991 [*16*] described DuPont's work-site health promotion efforts and estimated excess illness costs of $1,184 (CPI adjusted to 1998 dollars from $960), which represented only absenteeism and health care costs. Although this figure is below the $1,654 value used in the current model, it is above the model's sensitivity threshold for the benefit. Bertera further stated that his figures underestimate the costs of behavioral risk factors such as smoking, because of the tendency toward underestimation in self-reports of risky behaviors.

Warner et al. [*17*] in 1996 described a Monte Carlo simulation model that takes a long-term view (up to 85 years) of the costs and benefits of employer-based smoking cessation efforts. In their model, the benefits per successful quitter (as distinct from attempters, as in our model), even accounting for the background quit rate (i.e., those who would quit anyway, without a program), retirees, and others leaving the company, were estimated at $2,519 ($2,317 in 1995) by the fifth year of the program (although in the first few years there was a net loss). This figure is derived from absenteeism, medical care, and productivity savings ($1,034,076 in 1995)—much of which is not realized for those employees who leave—divided by the number of predicted successful quitters (446, including quitters who have left the company). Several of the assumptions of Warner et al. may explain their model's finding of an initial loss rather than gain. For example Warner et al. assumed that smokers use only 5 minutes per work day to smoke (vs 8 minutes, still a likely underestimate, in our model), that their intervention had an efficacy rate of 15% (vs 30% for Zyban), and that the employer accrued no health care savings or reductions in absenteeism during the first year.

A possible limitation in the present study is whether the data used in the model are generalizable. The quit rate data have high internal validity, in that they were from a well-controlled clinical trial with a placebo arm; however, because they are efficacy data, they may overestimate the quit rates obtainable in more real-life settings, in which less control is exercised over patient recruitment and compliance and in which patients may get less personal attention than in a clinical trial. It is also difficult at this time to ascertain whether the results with bupropion in this study are representative, as there is not a long history of clinical trials with this new agent as there is with nicotine patches, thus limiting comparisons with other published results. The results with NTP in our study, however, were similar to 1-year quit rates with the nicotine patch reported across study designs in a large meta-analysis [*18*]. The placebo rates in the current study are higher than published placebo rates. In the absence of inflated quit rates for the nicotine patch, this high placebo rate would suggest that any design-related bias would be against active treatment.

Another factor that could influence how generalizable the results are is the failure of the model to consider would-be quitters who attempt and fail several times before ultimately quitting smoking permanently. Smokers often require more than one attempt to quit, and this model does not account for such repeated attempts. However, the model used was the published base case, and because the model used efficacy data from a clinical trial in which additional quit attempts and further courses of treatment could not be undertaken, insufficient data were available to modify the base-case model to take subsequent attempts into account. It is unknown whether or how the effectiveness of bupropion may influence the number and frequency of subsequent quit attempts among relapsers, so the simpler *one-attempt-only* version of the model must remain our best approximation.

Another issue to consider is our use of point-prevalence abstinence rates rather than continuous abstinence rates in this analysis. Continuous abstinence rates are extremely conservative and require that a patient not smoke even a single cigarette during the

study in order to be considered abstinent. Many efficacy trials of pharmacotherapy report point-prevalence abstinence rates (usually within a standard period such as the preceding 1 to 2 weeks) as a realistic reflection of true quit rates. At least half of the studies in the 1994 meta-analysis of Fiore et al. [17] included point prevalence as the endpoint. A replication of the model using continuous abstinence data showed the same pattern of results as the current model and reached the same conclusions. In that replication, bupropion still accrued the highest net benefit ($141 for bupropion, versus $93 for placebo, $13 for bupropion plus NTP, and a net *loss* of $83 for NTP alone, for each quit attempt).

One further limitation that should be addressed is the absence of any costings associated with adverse events in the study. Indeed, the original model that we adapted also did not address adverse events, but the clinical study from which we derived our probabilities of successful quitting noted significantly higher occurrences of some adverse events in active groups relative to placebo. Of particular note was insomnia, which occurred in 30–48% of active group patients, compared with 20% of placebo patients. Although ideally an employer-focused model would assign productivity costs to a high-frequency adverse event, costing insomnia would be an arbitrary exercise, in that its effects on worker productivity have not been well-documented in the literature, and with most psychoactive medications insomnia tends to be transient. Patients in the trial received bupropion for only 9 weeks and yet were smoke-free for at least 1 year. Therefore, even if insomnia lasted for the entire treatment period, the amount of time that patients might have spent with insomnia is minimal compared with the lasting health and productivity effects associated with quitting smoking.

In summary, the findings of this study suggest that using bupropion in employee smoking cessation efforts could result in substantial savings for the employer. If we extrapolate our results to a hypothetical self-insured employer of 4,000 workers with an average smoking rate (i.e., 25% is the U.S. average[19]), and assume that 35% of all current smokers make an attempt to quit[20] using bupropion, the employer could save as much as $118,300 in the first post-quit year, even after paying for the full cost of the medication. This potentially represents a substantial economic benefit to employers who support smoking cessation programs in the workplace, as well as a general benefit to public health. Currently only approximately 25% of managed care plans pay for smoking-cessation interventions [21], but these findings suggest that companies whose plans pay for smoking cessation, even if funded directly from the company over and above current premiums, would reap substantial benefits.

CONCLUSION

The results of this economic decision analysis demonstrate that, from an employer's perspective, bupropion 300 mg/day for 9 weeks is a more cost-beneficial smoking-cessation intervention than the nicotine patch, with the potential to save employers up to $338 per smoker attempting to quit, in smoking-related illness and productivity costs in the first post-quit year. Benefits would continue to accrue for each year thereafter; however, the model used does not predict benefits beyond the short-term horizon of 1 year.

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