

# Cost-Effectiveness of Different Combinations of Bupropion SR Dose and Behavioral Treatment for Smoking Cessation: A Societal Perspective

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**Objectives:** To determine the differential cost effectiveness of 2 dosing regimens of bupropion sustained release (SR) in combination with behavioral interventions of minimal intensity (tailored mailings [TM]) or moderate intensity (proactive telephone calls [PTC]) for smoking cessation in an actual practice setting.

**Study Design:** Open-label, randomized trial, with 1-year follow-up, conducted in a large health system based in Seattle, Washington.

**Methods:** A total of 1524 adult smokers interested in quitting smoking were randomly assigned to receive 150 mg bupropion SR daily and PTC (n = 382), 150 mg bupropion SR daily and TM (n = 381), 300 mg bupropion SR daily and PTC (n = 383), or 300 mg bupropion SR daily and TM (n = 378). Sufficient medication for 8 weeks of dosing was provided to patients. The primary outcome measure was self-reported point-prevalence 7-day nonsmoking status at 12 months after the target quit date.

**Results:** Although the 300-mg dose was associated with a higher 12-month nonsmoking rate relative to the 150-mg dose with both PTC and TM, the additional cost resulted in lower cost effectiveness. The PTC behavioral intervention was more expensive than TM, but the additional effectiveness resulted in almost equivalent cost effectiveness at the 150-mg dose. Costs per additional 12-month nonsmoker (above that expected for placebo) for the 150-mg dose groups averaged \$950 and per additional lifetime quitter averaged \$1508; for the 300-mg groups these costs were \$1342 and \$2129, respectively. Cost per life-year and quality-adjusted life-years (QALYs) saved varied substantially by age and treatment, but were no greater than \$1100 for all treatment groups when averaged across the age and sex distribution for the study population.

**Conclusions:** Although the cost per life-year and QALYs saved were sufficiently low for all doses to rate these smoking cessation interventions as among the most cost effective of life-saving medical treatments, within the regimens tested 150 mg bupropion combined with either PTC or TM was the most cost effective.

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and colleagues,<sup>3</sup> Nielsen and Fiore<sup>4</sup> compared the cost-to-benefit ratio of bupropion sustained release (SR) at a dose of 300 mg per day with those of placebo, the nicotine transdermal patch (NTP), and a combination of bupropion SR plus NTP. The primary outcome evaluated was the point-prevalence rate of nonsmoking at 12 months of follow-up, and drug costs were based on the average wholesale price for bupropion SR and the NTP. All treatment arms received the same counseling, which included 9 supportive telephone calls, 9 weekly individual smoking-cessation counseling sessions, and relapse prevention counseling during 4 follow-up clinic visits. Even though intensive counseling was provided, Nielsen and Fiore estimated the midpoint cost for behavioral treatment (\$37.50) as if the behavioral intervention consisted of a single brief counseling session with a healthcare provider. (Essentially, Nielsen and Fiore conducted their cost analysis under the assumption that the smoking cessation rates for intensive and brief counseling would be the same.) Including costs for "brief medical counseling," the cost per 12-month nonsmoker for placebo, NTP, bupropion SR, and bupropion SR + NTP groups, were estimated to be \$240, \$1724, \$663, and \$1257, respectively.

The purpose of the present study was to examine the issue of cost effectiveness for smoking cessation treatment based on results from a large effectiveness trial of various combinations of bupropion and behavioral counseling in a healthcare setting. We assessed the effects of 2 doses of bupropion SR and 2 behavioral counseling approaches that would be more likely to be used in actual practice than the intense counseling in the Jorenby clinical trial.

Cigarette smoking has been associated with approximately 440 000 premature deaths in the United States annually during 1995 through 1999.<sup>1</sup> Although smoking cessation treatments are more cost effective than many other commonly provided clinical services,<sup>2</sup> obtaining the maximal benefits requires identification of cost-effective treatments. Using quit rates from a clinical efficacy trial reported by Jorenby

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**METHODS****Study Design**

Data used for the cost-effectiveness analyses were obtained from a field trial of the effectiveness of bupropion SR in an actual practice setting. The trial, conducted at Group Health Cooperative (GHC) in Seattle, Washington, consisted of 4 treatment groups defined by crossing 2 bupropion SR doses (150 and 300 mg per day) with 2 counseling approaches of varying intensity. The more intensive counseling program was the Free & Clear Program, which involved proactive telephone calls (PTC), and the less intensive program was a modified version of the Zyban Advantage Plan program, which relied primarily on tailored mailings (TM). A total of 1524 participants were enrolled and randomly assigned but not blinded to treatment. The primary outcome measure was self-reported point-prevalence 7-day nonsmoking status at 12 months after the target quit date (not biochemically confirmed). Using an intent-to-treat approach, we assigned the status of smoker to the 14.1% of participants who were survey nonrespondents. Details concerning trial methodology and trial outcomes are presented elsewhere.<sup>5,6</sup>

**Population Characteristics**

Participants, all members of GHC, were enrolled over a 13-month period between April 1998 and May 1999. GHC is a nonprofit consumer-governed healthcare system, headquartered in Seattle, Washington, serving approximately 600 000 residents of Washington State. The study was advertised in various publications mailed to GHC members and in brochures distributed to GHC clinics. Primary care physicians were informed of the study and were asked to refer eligible patients. A total of 2979 smokers interested in the study underwent detailed telephone screening; 1909 of these recruits were determined to be eligible. Inclusion and exclusion criteria were modeled after a previously conducted bupropion SR efficacy trial<sup>3</sup> and focused predominantly on conditions, including use of medications, that may lower seizure threshold. The pretreatment questionnaire and informed consent were obtained from 1524 smokers who were randomized into 1 of 4 treatment groups. Of the 385 smokers who did not end up in the final sample, 323 (84%) did not return their enrollment materials or subsequently refused participation, 23 (6%) were found not to have proper coverage, and the remaining 10% either reported exclusion criteria after screening or were excluded by their personal physician. The final sample of 1524 had an average age of 45.1 years, was 57.4% female, 89.7% white, had 13.7 years of formal schooling, smoked an average of 23.2 cigarettes per day for an

average of 26.5 years, and had made 5.9 previous quit attempts. Approximately one-third (30.7%) had previously quit for 6 or more months, and most (63.3%) had previously used nicotine patches or gum.

**Interventions**

In the PTC program, all registrants received an outgoing call from a smoking cessation counselor a few days before the estimated quit date. After this call an average of 4 follow-up outgoing calls were made, each taking an average of 11.5 minutes (including time for unsuccessful call attempts), with follow-up letters being sent after 3 unsuccessful attempts to complete a call. Participants could also call an ad hoc support line, with an average usage of 21 minutes per enrollee. In the TM program, the participant was sent an individualized action plan prior to the quit date. On the quit date, the participant received a scripted outgoing call from a customer service representative. At 1, 8, 11, and 24 weeks after the quit date, participants received brief questionnaires that could be completed by mail or by using an automated, interactive voice-response telephone system. Participants who responded to a questionnaire were mailed a tailored relapse prevention/recovery plan. In addition, participants could access an automated tip line or talk to a program specialist; these latter interactions averaged just under a minute (54 seconds) per enrollee.

**Cost Estimates**

Costs for the various components were estimated (as of January 2003) based on the amount and type of personnel time involved, wage rates and overhead benefits, facilities costs, time spent on indirect tasks related to an ongoing smoking cessation behavioral intervention program (departmental meetings, quality control activities, etc), telephone costs, management costs, printing, and postage. Drug costs were estimated based on contract pricing, pharmacy dispensing costs, and allocable pharmacy overhead. Costs were not included for advertising, training or informing physicians or other medical staff, staff hiring and training, program development costs, materials development costs, or information technology infrastructure investment, because these would be primarily nonrecurring costs. Based on Bureau of Labor Statistics regional employment cost indices for March 2003, differences in regional employment costs could alter the costs of the behavioral intervention by -2.4% (for the South) to +0.6% (for the Midwest).

**Cost-effectiveness Calculations**

Meta-analyses of smoking cessation studies<sup>4,7,8</sup> have shown that control group cessation rates range from

6% to 12%. To adjust for the background quit rates among smokers who are motivated to quit, a 12-month "placebo-adjusted" nonsmoking rate was calculated by subtracting 11% from the observed 12-month nonsmoking rates.

The cost per additional nonsmoker at 12 months was derived by dividing the cost per enrollee by the 12-month placebo-adjusted quit rate. The incremental cost per 12-month quitter for various treatment pairs was also calculated. Previous research<sup>9,10</sup> had estimated a 35% to 40% lifetime probability of relapse from smoking cessation after 1 year of abstinence, so lifetime nonsmoking rates were calculated assuming a 37% relapse rate.

The cost effectiveness of the interventions in increasing life expectancy was calculated using the mortality rates given by Croghan and associates.<sup>11</sup> The impact of smoking on health-related quality of life was calculated using the Healthy People 2000 years of healthy life measure,<sup>9,12</sup> extrapolating the measures down to age 18 years and up to 100 years using piecewise linear extrapolation.

Estimates in the literature for spontaneous quit rates for smokers range from 0.5% to 2.5%.<sup>9,10,13-15</sup> Historical estimates for the spontaneous quit rate were used to minimize the portion of spontaneous quits that were aided (ie, through physician counseling, use of prescription or over-the-counter nicotine replacement aids, telephone quit lines, etc). For cost-estimation purposes, we estimated the rate of spontaneous unaided quits followed by a minimum of 12 months of reported nonsmoking to be 1.5%. (However, because this rate may now be higher as a result of increased awareness of the deleterious effects of tobacco, we also examined the effect of increasing the unaided spontaneous quit rate to 2.5% and 3.5%.) Spontaneous quitters who remained nonsmokers for at least 12 months were also subject to later relapse using the 37% relapse rate described above.

The cost per life-year saved was calculated as the cost per lifetime quitter divided by the number of life-years saved per lifetime quitter. The latter quantity was estimated by subtracting the number of life-years remaining for a lifetime quitter of a specified sex and age (at the time of quitting) by the number of life-years remaining for a current smoker of the same sex and age. Monte Carlo simulation was used to estimate the number of life-years remaining for a current smoker, taking into account the possibility each year that a smoker would permanently quit without assistance, and the appropriate mortality rates based on that smoker's age, sex, and years since quitting (if any). The cost per quality-adjusted life-year (QALY) was similarly estimated. Both calculations used a 3% discount rate for future life-years and QALYs.

Economic analyses of the medical costs of smoking have shown conflicting findings.<sup>16-22</sup> Given the difficulties inherent in demonstrating a net lifetime medical cost advantage to smoking cessation, we have not attempted to estimate the corresponding cost advantage.

RESULTS

**Years of Life and Quality-adjusted Life-years Saved**

The years of life (YOL) saved after smoking cessation are shown under 6 different scenarios in **Table 1**. Without adjusting (discounting) for the spontaneous quit rate of smokers (scenario A), smoking cessation saves between 2.16 and 9.11 life-years for men and between 2.91 and 9.09 life-years for women. Using the age and sex distribution of participants in our study, the average YOL saved would be 7.83 years. Discounting by 3% (scenario B) reduces the average YOL saved to 2.60. Adjusting for the estimated spontaneous unaided quit rate of smokers (1.5%) (scenario C) reduces the average YOL saved to 2.17. Increasing the spontaneous unaided quit rate to 2.5% (scenario D) or 3.5% (scenario E) reduces the average YOL saved to 1.89 and 1.72, respectively. Discounting by 5% (scenario F) reduces the average YOL saved to 1.17. The pattern for QALYs (shown in **Table 2**) is similar to that for YOL saved, with larger variability across age than YOL saved when discounting is not used and smaller variability when discounting is used.

**12-Month and Lifetime Cessation Rates, and Related Costs**

Study results in the baseline scenario with respect to cost per abstainer are presented in **Table 3**. Although the 300-mg dose groups exhibited slightly larger 12-month nonsmoking rates (33.2% with PTC and 25.7% with TM) than the 150-mg dose groups (31.4% with PTC and 23.6% with TM), these differences were not statistically significant (either within or across behavioral intervention). The groups using the TM program had statistically significantly lower 12-month placebo-adjusted cessation rates (12.6% and 14.7%) than the PTC groups (20.4% and 22.2%;  $z > 2.11, P < .05$ ). The order of the groups by 12-month placebo-adjusted cessation rate was also the order of the groups by total cost per enrollee, which ranged from \$119 to \$283. When costs were expressed per additional 12-month abstainer (above the number expected from placebo), the 150-mg/TM and 150-mg/PTC groups had almost identical cost effectiveness (\$944 and \$956). Relative to 150 mg/TM, the incre-

**Table 1.** Years of Life Saved Because of Smoking Cessation, by Scenario, Sex, and Age

	% in Study*	Scenario					
		A	B	C	D	E	F
Discount rate (%)		0.0	3.0	3.0	3.0	3.0	5.0
Yearly quit rate (%) <sup>†</sup>		0.0	0.0	1.5	2.5	3.5	1.5
Relapse rate (%) <sup>‡</sup>		0.0	0.0	37.0	37.0	37.0	37.0
Men, age range (y)							
18-24	1.8	9.11	1.74	1.22	0.98	0.83	0.45
25-34	6.2	8.65	2.10	1.64	1.45	1.14	0.70
35-44	12.5	8.34	2.66	2.19	1.87	1.66	1.09
45-54	13.5	7.79	3.18	2.77	2.39	2.33	1.60
55-64	6.8	5.97	3.05	2.84	2.53	2.41	1.86
65-74	1.6	3.88	2.44	2.41	2.29	2.13	1.79
75-85	0.2	2.16	1.61	1.52	1.51	1.50	1.23
Women, age range (y)							
18-24	3.0	9.09	1.45	1.02	0.80	0.63	0.36
25-34	9.4	8.87	1.90	1.37	1.05	0.86	0.55
35-44	17.7	8.46	2.34	1.88	1.58	1.35	0.86
45-54	16.5	7.87	2.81	2.30	2.09	1.88	1.21
55-64	7.5	6.86	3.14	2.82	2.45	2.57	1.73
65-74	2.8	5.03	2.87	2.63	2.52	2.30	1.83
75-85	0.6	2.91	2.04	1.84	1.76	1.74	1.46
Average across age and sex		7.83	2.60	2.17	1.89	1.72	1.17

Scenarios A–F refer to percentages of discounting, or adjusting, for the spontaneous quit rate of smokers. A = 0%; B = 3%; C = 1.5%; D = 2.5%; E = 3.5%; F = 5%. Years of life saved are estimated for ages 20, 30, 40, 50, 60, 70, and 80.

\*The distribution across ages and sex in the study population.

<sup>†</sup>Yearly probability that an unaided smoker will quit for 12 months.

<sup>‡</sup>Probability that an unaided smoker who has quit for 12 months will subsequently relapse.

mental cost effectiveness of 150 mg/PTC was \$974, and for the 300-mg groups was \$1708 (PTC) and \$4190 (TM). The costs per lifetime quitter ranged from \$1499 to \$2235 across the 4 groups.

**Cost per Life-year and Quality-adjusted Life-years Saved**

Study results with respect to cost per YOL saved under baseline assumptions are shown in **Table 4**. The cost per YOL saved varied by age and sex with generally less cost effectiveness at young ages (because mortality rates are low for both smokers and nonsmokers and future YOL saved are heavily discounted) and at older ages (because fewer YOL remain). Costs per YOL saved ranged from \$528 to \$2194. The incremental costs per YOL saved versus 150-mg/TM (that is, the cost per additional YOL saved beyond that which would be achieved

using 150-mg/TM treatment) were reasonable for the 2 PTC groups (\$712 for the 150-mg group and \$1248 for the 300-mg group), whereas those for the 300-mg/TM group were substantially higher (\$3061). Costs per QALY saved followed the same pattern by treatment group but showed less variability by age.

**Sensitivity Analysis**

We examined the sensitivity of our results to parameter values by developing 2 scenarios that modified parameters so as to minimize or maximize cost effectiveness (denoted as the pessimistic and optimistic scenarios), as shown in **Table 5**. Under the pessimistic scenario (see upper half of **Table 6**), the cost per each additional 12-month quitter (above the expected rate in a placebo group) ranged from \$1525 to \$2515. The cost per lifetime quitter ranged from \$2824 to \$4657. In this

**Table 2.** QALYs Saved by Smoking Cessation, by Scenario, Sex, and Age

% in Study*	Scenario						
	A	B	C	D	E	F	
Discount rate (%)	0.0	3.0	3.0	3.0	3.0	5.0	
Yearly quit rate (%) <sup>†</sup>	0.0	0.0	1.5	2.5	3.5	1.5	
Relapse rate (%) <sup>‡</sup>	0.0	0.0	37.0	37.0	37.0	37.0	
Men, age range (y)							
18-24	1.8	10.12	2.60	1.98	1.66	1.45	0.96
25-34	6.2	9.37	2.97	2.44	2.18	1.86	1.32
35-44	12.5	8.45	3.24	2.76	2.43	2.21	1.61
45-54	13.5	7.21	3.29	2.93	2.58	2.50	1.85
55-64	6.8	5.13	2.78	2.61	2.36	2.25	1.79
65-74	1.6	3.07	1.98	1.95	1.86	1.75	1.48
75-85	0.2	1.55	1.17	1.09	1.11	1.10	0.91
Women, age range (y)							
18-24	3.0	8.71	2.00	1.54	1.29	1.09	0.75
25-34	9.4	8.19	2.32	1.83	1.51	1.31	0.96
35-44	17.7	7.38	2.49	2.09	1.81	1.61	1.15
45-54	16.5	6.39	2.56	2.17	1.99	1.81	1.27
55-64	7.5	5.18	2.52	2.28	2.08	2.01	1.47
65-74	2.8	3.56	2.09	1.92	1.84	1.69	1.37
75-85	0.6	1.94	1.38	1.24	1.19	1.18	1.00
Average across age and sex		7.07	2.70	2.31	2.05	1.88	1.38

Scenarios A–F refer to percentages of discounting, or adjusting, for the spontaneous quit rate of smokers. A = 0%; B = 3%; C = 1.5%; D = 2.5%; E = 3.5%; F = 5%. QALYs saved are estimated for ages 20, 30, 40, 50, 60, 70, and 80.

\*The distribution across ages and sex in the study population.

<sup>†</sup>Yearly probability that an unaided smoker will quit for 12 months.

<sup>‡</sup>Probability that an unaided smoker who has quit for 12 months will subsequently relapse.

QALY indicates quality-adjusted life-year.

**Table 3.** Cost Effectiveness With Respect to 12-month and Lifetime Nonsmoking Rates Using Baseline Estimates

	Bupropion–Counseling Combined Therapy			
	PTC		TM	
	150 mg (n = 382)	300 mg (n = 383)	150 mg (n = 381)	300 mg (n = 378)
12-month nonsmoking rate (%)	31.4	33.2	23.6	25.7
Incremental 12-month nonsmoking rate (%) <sup>*</sup>	20.4	22.2	12.6	14.7
(95% CI)	(16.4–24.4)	(18.0–26.4)	(9.3–15.9)	(11.1–18.3)
Lifetime nonsmoking rate (%)	12.9	14.0	7.9	9.3
(95% CI)	(10.3–15.4)	(11.4–16.6)	(5.8–10.0)	(7.0–11.5)
Cost of interventions per enrollee (\$)				
Behavioral intervention (\$)	104	104	28	28
Bupropion costs (\$)	91	179	91	179
Total cost per enrollee (\$)	195	283	119	207
Cost per additional nonsmoker at 12 months (\$)	956	1275	944	1408
Incremental cost per additional nonsmoker at 12 months vs 150 mg/TM (\$)	974	1708	—	4190
Cost per lifetime quitter (\$)	1517	2023	1499	2235
Incremental cost per lifetime quitter vs 150 mg/TM (\$)	1547	2712	—	6652

\*Calculated by subtracting the 12-month nonsmoking rate for placebo (11%) from the 12-month nonsmoking rate for that treatment group. PTC indicates proactive telephone calls; QALY, quality-adjusted life-year; SR, sustained release; TM, tailored mail.

**Table 4.** Cost Effectiveness With Respect to YOL and QALYs Saved Under Baseline Assumptions

	Bupropion-Counseling Combined Therapy			
	PTC		TM	
	150 mg	300 mg	150 mg	300 mg
<b>Cost per life-year saved (\$)</b>				
Men, age at start of lifetime quit (y)				
20-29	1239	1652	1224	1825
30-39	924	1232	913	1361
40-49	694	925	686	1022
50-59	547	729	540	806
60-69	534	713	528	787
70-79	630	841	623	929
80-89	1019	1359	1006	1501
Women, age at start of lifetime quit (y)				
20-29	1490	1987	1472	2194
30-39	1105	1473	1092	1627
40-49	808	1077	798	1190
50-59	659	879	652	972
60-69	539	719	532	794
70-79	577	769	570	850
80-89	826	1101	816	1216
Average across sex and ages	747	997	739	1101
<b>Cost per QALY saved (\$)</b>				
Men, age at start of lifetime quit (y)				
20-29	768	1024	758	1131
30-39	622	829	614	916
40-49	550	733	543	810
50-59	519	691	512	764
60-69	582	777	575	858
70-79	777	1037	768	1145
80-89	1390	1853	1373	2047
Women, age at start of lifetime quit (y)				
20-29	985	1314	973	1451
30-39	831	1108	821	1224
40-49	727	970	719	1071
50-59	700	934	692	1032
60-69	666	888	658	981
70-79	789	1052	780	1162
80-89	1219	1626	1205	1796
Average across sex and ages	698	931	690	1029
<b>Incremental cost for distribution of ages and sex in the study population (\$)</b>				
For life-years vs 150 mg/TM (\$)	712	1248	—	3061
For QALYs vs 150 mg/TM (\$)	669	1173	—	2877

PTC indicates proactive telephone calls; QALY, quality-adjusted life-year; SR, sustained release; TM, tailored mail, YOL, years of life.

scenario, 150 mg/PTC is somewhat more cost effective than 150 mg/TM, the opposite of the situation under the baseline scenario. The cost per YOL saved ranged from \$2605 to \$4295 and the cost per QALY saved ranged from \$2177 to \$3590. Under the optimistic scenario

(see lower half of Table 6), the cost for each additional 12-month abstainer (above the expected rate in a placebo group) ranged from \$560 to \$861, and the cost per lifetime quitter ranged \$756 to \$1164. The cost per YOL saved ranged from \$106 to \$163 and the cost per QALY

saved range from \$116 to \$179.

**Comment**

The cessation rates we found after treatment with various combinations of bupropion and counseling in the present study were comparable to those reported by Nielsen and Fiore.<sup>4</sup> The costs of the behavioral interventions in our study (\$28 for TM and \$104 for PTC) were similar to costs cited in the literature for other comparable programs (\$26 and \$148).<sup>23</sup> The costs for the 300-mg groups in our study were somewhat higher than those calculated by Nielsen and Fiore<sup>4</sup> because of the higher costs for the TM and PTC treatments relative to the authors' underestimated costs of intervention in the Jorenby study. No group in our study was as expensive as their bupropion + NTP group (\$446 per enrollee), nor as inexpensive as their placebo group (\$38 per enrollee, including counseling costs).

The costs per lifetime quitter in our study (\$1499 to \$2235) were lower than those reported by Cromwell and associates<sup>24</sup> for placebo, nicotine gum, or NTP combined with 5 levels of counseling intensity. Their costs ranged from a low of \$2186 for group intensive counseling without nicotine replacement to a high of \$8962 for nicotine gum with minimal counseling. The cost per YOL saved (after adjusting for placebo) in our study was generally lower than those reported in the smoking cessation literature,<sup>9,13,14,24,25</sup> and considerably lower for the 150-mg dose groups (an average of \$700 less). Thus, 150 mg bupropion combined with either PTC or TM would appear to be one of the most cost-effective smoking cessation treatments available.

The smoking cessation interventions in our study also compared favorably with other generally accepted preventive health strategies with respect to cost per YOL saved.<sup>9,17,26-29</sup> Tengs and co-workers<sup>26</sup> reviewed 500 life-saving interventions, and after adjusting for inflation (to 1993 dollars), discount rate (5%), and excluding indirect costs, the median intervention cost was \$42 000 per life-year saved. Warner<sup>30</sup> stated "a life-year saved at a cost of less than \$20 000 (the highest cost estimate in the smoking-cessation treatment liter-

ature) constitutes a very worthwhile investment." In addition, as noted by Oster and associates,<sup>14</sup> the relative cost effectiveness of smoking cessation treatments may be underestimated because the treatments are relatively brief and incur only relatively minor adverse effects. Under the optimistic scenario the cost per YOL and QALY saved range from \$106 to \$179, putting these treatments into the cost effectiveness neighborhood of vaccines.

As impressive as the cost-effectiveness measures were for our 150-mg dose groups, they might be improved. Because a substantial portion of total costs were attributable to the pharmacotherapy, and because smoking cessation trials show that smoking during the first 1 or 2 weeks of NTP therapy is predictive of relapse,<sup>31-33</sup> we speculate that the cost effectiveness of bupropion treatment might be improved by having physicians initially prescribe a 3-week supply of bupropion SR with a recommendation that the patient fill a subsequent prescription for an additional 5 weeks only if he or she remains abstinent for the initial 3-week time period. In addition, bupropion is still patent protected. When the patent expires and the formula becomes available generically, historical experience with other medications suggests that the costs will decline. Using current prices, however, we concluded that following the manufacturer's recommendation of

Table 5. Parameters Used in Sensitivity Analysis

Parameter	Cost-effectiveness Scenario		
	Baseline	Pessimistic	Optimistic
12-month nonsmoking rates (%)			
Spontaneous unaided yearly quit rate	1.5	2.5	0.5
Motivated smokers on placebo	11.0	15.4	7.7
150 mg/PTC	31.4	26.7	36.1
300 mg/PTC	33.2	28.5	37.9
150 mg/TM	23.6	19.3	27.9
300 mg/TM	25.7	21.3	30.1
Cost of PTC (\$)	104	130	78
Cost of TM (\$)	28	35	21
Cost of 150 mg bupropion SR (\$)	91	114	68
Cost of 300 mg bupropion SR (\$)	179	224	134
Relapse rate for 12-month quitters (%)	37.0	46.0	26.0
Discount rate for life-years and QALYs (%)	3.0	5.0	0.0

PTC indicates proactive telephone calls; QALY, quality-adjusted life-year; SR, sustained release; TM, tailored mail.

**Table 6.** Cost Effectiveness Using Pessimistic and Optimistic Scenarios

	Bupropion-Counseling Combined Therapy			
	PTC		TM	
	150 mg	300 mg	150 mg	300 mg
<b>Pessimistic Scenario</b>				
Incremental 12-month nonsmoking rate (%)*	16.0	17.8	8.2	10.3
Lifetime nonsmoking rate (%)	8.6	9.6	4.4	5.6
Cost of interventions per enrollee (\$)				
Behavioral intervention	130	130	35	35
Bupropion costs	114	224	114	224
Total cost per enrollee	244	354	149	259
Cost per additional abstainer at 12 months (\$)	1525	1989	1817	2515
Cost per lifetime quitter (\$)	2824	3683	3365	4657
Cost per life-year saved (\$)†	2605	3397	3104	4295
Cost per QALY saved (\$)†	2177	2840	2594	3590
<b>Optimistic Scenario</b>				
Incremental 12-month nonsmoking rate (%)*	23.7	25.5	15.9	18.0
Lifetime nonsmoking rate (%)	17.5	18.9	11.8	13.3
Cost of interventions per enrollee (\$)				
Behavioral intervention	78	78	21	21
Drug costs	68	134	68	134
Total cost per enrollee	146	212	89	155
Cost per additional abstainer at 12 months (\$)	616	831	560	861
Cost per lifetime quitter (\$)	832	1123	756	1164
Cost per life-year saved (\$)†	116	157	106	163
Cost per QALY saved (\$)†	128	172	116	179

\*Calculated by subtracting the 12-month nonsmoking rate for placebo from the 12-month nonsmoking rate for that treatment group.

†Averaged across the age and sex distribution of the study population.

PTC indicates proactive telephone calls; QALY, quality-adjusted life-year; TM, tailored mail.

using a 300-mg dose will result in a less cost-effective program than use of a 150-mg dose. (The manufacturer's recommendation for dose appears to be based on a comparison of the 6-week continuous abstinence rates for doses of placebo, 100, 150, and 300 mg bupropion. In the clinical trial<sup>34</sup> providing the 6-week continuous abstinence rates, no statistically significant difference was noted in the point-prevalence rates at 12 months for 150 and 300 mg bupropion [22.9% and 23.1%, respectively], and the trial did not consider medication costs or cost effectiveness.)

Discounting has a substantial effect on the relative benefit of smoking cessation in increasing YOL saved for different age groups. Without discounting, lifetime smoking cessation for a 20-year old man resulted in a savings of 9.11 life-years, whereas smoking cessation for a 70-year old man resulted in a savings of only 3.88 life-years. However, with a discount rate of 3.0%, the savings advantage was reversed. These facts resulted in the counterintuitive finding that smoking cessation

programs should be directed to the elderly to be most cost effective, even though, in the very long term, treating 1 000 000 young smokers per year would yield a greater YOL savings than treating an equal number of elderly smokers.

The findings of this study should be interpreted cautiously because of limitations inherent in the methodology and assumptions. The data used to derive mortality rates for quitters was derived from the Cancer Prevention Study II (CPS II) database, and the participants in that study are generally acknowledged to be healthier than the general US population. This will tend to result in an overestimation of YOL saved for the general population (although not necessarily for managed care populations of generally healthy individuals). However, no adequate method for adjusting for the better health status of the CPS II population (relative to the general US population) is apparent. Estimates of mortality rates were extrapolated to ages younger than 45 years and older than 79 years and

quality of life was extrapolated to ages younger than 25 years and older than 69 years. Extrapolation involves assumptions concerning the applicability of relationships observed in some age groups to other age groups and may not be accurate.

The study sample used in these analyses was predominantly Caucasian and middle class, and consisted of volunteers who knew that they would receive bupropion SR. Smoking cessation rates achieved in this population may not be reflective of smoking cessation rates among the general population. The study also was not blinded, and did not include a placebo group or biochemical verification of smoking cessation. Biochemical verification would presumably have resulted in somewhat lower cost effectiveness, although the literature suggests that the rate of underreporting of smoking in a field trial of this type may be minimal.<sup>35-37</sup> For the field trial, an intent-to-treat approach was used to code nonrespondents as smokers. This tactic may have led to slightly decreased 12-month cessation rates and estimates of cost effectiveness.

No adverse effects requiring hospitalization were reported in this study. Four patients were seen in the emergency department (although none with as serious a condition as anaphylaxis). Had costs for emergency department visits been included, cost effectiveness would have been slightly lower. In addition, an increase in minor adverse effects (such as insomnia) was seen with higher levels of bupropion SR. Given the transience of the minor adverse effects and the availability of written material and counselors to explain these effects, medical expenses associated with the minor adverse effects were probably minimal.

Our baseline scenario assumed a constant spontaneous unaided yearly quit rate of 1.5%. Other research<sup>38</sup> suggests that quit rates increase with age. However, some of this increase may be due to poorer health status with increasing age, increased interventions by physicians to encourage their patients to stop smoking, or greater use of smoking cessation aids. More research is necessary to quantify the relationship between the spontaneous unaided quit rate and age.

In summary, smoking cessation treatment consisting of 150 mg bupropion combined with an intensive telephone-based counseling program or a less intensive tailored mailing counseling program were approximately equally cost effective, were more cost effective than treatments using a 300-mg dose, and were more cost effective than many other smoking cessation interventions discussed in the literature. Cost per YOL and QALY saved, which were less with the 150-mg dose than the 300-mg dose, were sufficiently low for all

doses to rate any of these smoking cessation interventions as among the most cost effective of life-saving medical treatment.

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