Cost-Effectiveness of Smoking Cessation Treatment Initiated During Psychiatric Hospitalization: Analysis From a Randomized, Controlled Trial

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ABSTRACT

Objective: We examined the cost-effectiveness of smoking cessation treatment for psychiatric inpatients.

Method: Smokers, regardless of intention to quit, were recruited during psychiatric hospitalization and randomized to receive stage-based smoking cessation services or usual aftercare. Smoking cessation services, quality of life, and biochemically verified abstinence from cigarettes were assessed during 18 months of follow-up. A Markov model of cost-effectiveness over a lifetime horizon was constructed using trial findings and parameters obtained in a review of the literature on quit and relapse rates and the effect of smoking on health care cost, quality of life, and mortality.

Results: Among 223 smokers randomized between 2006 and 2008, the mean cost of smoking cessation services was $189 in the experimental treatment group and $37 in the usual care condition ($P < .001$). At the end of follow-up, 18.75% of the experimental group was abstinent from cigarettes, compared to 6.80% abstinence in the usual care group ($P < .05$). The model projected that the intervention added $43 in lifetime cost and generated 0.101 additional quality-adjusted life-years (QALYs), an incremental cost-effectiveness ratio of $428 per QALY. Probabilistic sensitivity analysis found the experimental intervention was cost-effective against the acceptance criteria of $50,000/QALY in 99.0% of the replicates.

Conclusions: A cessation intervention for smokers identified in psychiatric hospitalization did not result in higher mental health care costs in the short-run and was highly cost-effective over the long-term. The stage-based intervention was a feasible and cost-effective way of addressing the high smoking prevalence in persons with serious mental illness.

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Individuals with mental health disorders are at least twice as likely to smoke as persons without mental illness[1] and consume more cigarettes than other smokers.[2–4] Persons with serious mental illness (SMI), including schizophrenia, bipolar disorder, and severe and chronic depression, have much higher age-adjusted mortality rates than the rest of the population.[5–7] High smoking prevalence and high rates of smoking-related illness contribute to this elevated risk.[5]

Pharmacologic and behavioral cessation treatments for smokers with SMI have been found effective in clinical trials, with quit rates between 4% and 22%.[8] Bupropion and varenicline have been shown to be effective cessation pharmacotherapies in smokers with schizophrenia.[9–11] Initiation of tobacco cessation during medical hospitalization is effective,[12] but trials have not been conducted in psychiatric hospitals. The inpatient psychiatric setting is a promising venue to identify smokers with SMI who may be ready to quit. Most psychiatric hospitals are now smoke-free environments and many provide hospitalized smokers with nicotine replacement therapy (NRT), giving patients a trial period of abstinence supported by pharmacotherapy, but hospitals are not yet availing themselves of this opportunity to treat nicotine dependence.[13]

Smoking cessation in other populations provides sufficient value to justify the cost of treatment, with a cost-effectiveness ratio well below the $50,000 per quality-adjusted life-year (QALY) threshold often used in the United States.[14–19] It does not follow that cessation services will be cost-effective for smokers with SMI, who tend to have lower quit rates than other smokers[2,20] and may require more intensive cessation services. The incremental value of quitting is attenuated by the lower quality of life[21] and higher mortality rates from causes other than smoking in patients with SMI.[5] The cost-effectiveness of smoking cessation for patients with SMI has not been determined,[8] a gap addressed by this article.

A previously reported randomized clinical trial[22] among patients recruited from a locked acute inpatient psychiatry unit with a complete smoking ban supported by NRT found a sustained tobacco treatment program resulted in significantly greater abstinence from tobacco during 18 months of follow-up. We now report the cost of the treatment, its effect on utilization and cost of mental health services in the short-run, and its cost-effectiveness over the long-term.

METHOD

Adult inpatients in a smoke-free psychiatric care unit, the Langley Porter Psychiatric Institute at the University of California San Francisco, were recruited and randomized to standard care or

Clinical Points

- A smoking cessation intervention for cigarette smokers identified during psychiatric hospitalization was highly cost-effective according to criteria used to evaluate the adoption of health care interventions in the United States.
- There was no evidence that the intervention increased the utilization or cost of mental health services.
- Although persons with psychiatric illness have lower quality of life and increased mortality from nonsmoking causes, directing smoking cessation programs to persons with mental illness does not mean that tobacco control efforts will become less efficient.

a stage-tailored smoking cessation intervention[22] (registered at ClinicalTrials.gov: NCT00136812). All participants received NRT to manage withdrawal during hospitalization. Standard care consisted of a smoking cessation pamphlet provided during hospitalization and brief advice to quit. The experimental interventions included a computer-assisted assessment of stage of change and other major constructs of the transtheoretical model (ie, decisional balance, temptations, and processes of change) with tailored feedback administered during the hospital stay and 3 and 6 months later. Feedback at the later sessions highlighted changes from the earlier assessments. Printed feedback reports were provided to the participants and mailed to their outpatient providers. Participants in the experimental intervention group also received a stage-tailored workbook, met with a study counselor on the unit for 15–30 minutes, and were offered up to 10 weeks of NRT in the form of transdermal patch for use after hospitalization.

Informed consent was obtained under an institutional review board–approved protocol. Smoking status was assessed at 3, 6, 12, and 18-month follow-up regardless of treatment status by using participant-reported 7-day abstinence verified by carbon monoxide testing and collateral report.

Cost of Smoking Cessation Services

The cost of NRT was estimated as the retail price. The cost of other cessation pharmacotherapies was the acquisition cost of the US Medicaid program,[23] 65% of the average wholesale price.[24] Each computer assessment was assigned a pro rata share of the computer, software, and technical assistance. Labor costs were $22/h, including wages and benefits. Self-reported cessation services obtained outside the study were assigned the unit cost of study-provided services or else a unit cost obtained from literature review.

Health Services Utilization and Cost

We obtained the quantity and cost of mental health care obtained by trial participants in the 18 months of study follow-up and used a long-term model to estimate the cost of medical services.

We obtained utilization and charge data from the recruitment site. Participants reported medications used and mental health services received from other providers, and provided releases to obtain bills for psychiatric hospitalization. Inpatient charges were adjusted by the hospital's cost-to-charge ratio. Outpatient visits were assigned the mean cost of that service at the study site. Medication costs were estimated as Medicaid acquisition cost. We included all costs from discharge from the hospital stay where participants were randomized until the end of follow-up.

Group differences in health care utilization were compared using a negative binomial regression. Differences in cost were compared using a γ regression with log link function.

Quality of Life

Quality of life was assessed with the 12-item Medical Outcomes Study Short-Form (SF-12),[25] scored with preference-based utility weights.[26] We estimated the effect of mental illness and other nonsmoking factors on quality of life by dividing the utility of the final assessment of each participant by the utility of a population of primary care patients matched by age and smoking status.[27]

Model

We used a lifetime model to project the effect of smoking cessation on health care cost and morbidity adjusted survival. The QALY is the standard measure defined so that improvements in survival and quality life can be represented on a single scale. Years of life are adjusted for their quality, measured in units of preference-based utility, a measure that spans a range from 0 (representing death) to 1 (representing perfect health). The difference in cost between experimental and control conditions was divided by the difference in QALYs to determine the incremental cost effectiveness ratio, or the cost incurred per QALY realized, a widely used measure of efficiency.

We constructed a Markov model to project the effect of smoking cessation on future smoking status and the associated quality of life, health care costs, and mortality. During each model cycle, current smokers may quit, former smokers may relapse, and members of either group may die. The model tallies the costs and QALYs that are realized by each randomization group, given their initial smoking status, over a lifetime horizon (until all smokers and former smokers have died).

The model used trial data on participant age, the effect of mental health on quality of life, the initial cost of smoking cessation services, and smoking status at the end of follow-up. Other parameters used in the model are presented in Table 1.

We found the spontaneous cessation rate of smokers to be 4.3% per year,[28] and the relapse rate among quitters to be 15.0% in the first year after a sustained 1-year quit[31] and diminishing in subsequent years.[30–33] We assumed a relapse rate that was 150% higher, as former smokers with psychiatric illness are more likely to relapse than other smokers.

We estimated mortality rates by applying published hazard ratios for smokers and former smokers to age-specific US mortality rates of never smokers.[34–37] The extra

Table 1. Model Parameters for Changes in Smoking Status, Mortality, Quality of Life, and Cost Obtained From Literature Review

Parameter	Parameter Value	Reference Source
Quit rate among current smokers (% per year)	4.3%	28, 29
Relapse rate among former smokers after 1 year of abstinence (% per year)		30–33
Year 2 after initial quit	15%	
Year 3–5 after initial quit	5%	
Year 6–9 after initial quit	2%	
Year 10+ after initial quit	1%	
Excess mortality relative to never smokers (hazard ratio)		34–37
Female current smokers age 24–54	1.369	
Female current smokers age 55–74	2.533	
Female current smokers age 75+	1.411	
Female former smokers age 24–54	1.214	
Female former smokers age 55–74	1.666	
Female former smokers age 75+	1.111	
Male current smokers age 24–54	2.486	
Male current smokers age 55–74	2.550	
Male current smokers age 75+	1.326	
Male former smokers age 24–54	1.074	
Male former smokers age 55–74	1.992	
Male former smokers age 75+	1.074	
Excess mortality from non-smoking causes (hazard ratio)		
Smoking mortality hazard in schizophrenia	1.65	5
All-cause mortality hazard in schizophrenia	2.5	6
Nonsmoking mortality hazard in depression	1.3	7
Quality of life (preference-based utilities)		27
Female moderate smokers age 55–64	0.7648	
Female moderate smokers age 65–74	0.7520	
Female moderate smokers age 75+	0.6778	
Female former smokers age 55–64	0.7827	
Female former smokers age 65–74	0.7709	
Female former smokers age 75+	0.6987	
Male moderate smokers age 55–64	0.7815	
Male moderate smokers age 65–74	0.7575	
Female moderate smokers age 55–64	0.7112	
Male former smokers age 55–64	0.8020	
Male former smokers age 65–74	0.7802	
Male former smokers age 75+	0.7358	
Health care charges incurred by smokers and former smokers relative to the general population (relative charges)		38
Smokers	1.1881	
Recent quitters (< 5 years)	1.2476	
Long-term quitters (5+ years)	0.9595	
Annual health care cost (2010 US$)		39
Female age 18–24	2,235	
Female age 25–44	3,347	
Female age 45–64	6,229	
Female age 65–90	9,623	
Male age 18–24	1,072	
Male age 25–44	2,158	
Male age 45–64	5,217	
Male age 65–90	10,249	

nonsmoking mortality risk associated with mental illness was based on review of literature on all-cause and smoking-related mortality in different illnesses[5–7] weighted by the mix of illnesses among trial participants.

The model used a 3-month cycle, the minimum interval between study follow-up assessments. It was calibrated by comparing its projection of expected years of life at the time of a permanent quit in smokers in the general population to published reports.[40,41]

We used published age- and gender-specific estimates of quality of life.[27] We estimated the effect of smoking on annual health care costs. We used age- and gender-specific health care costs from a national survey,[39] and adjusted these for the relative effect of smoking status on health care charges in a study of a large employer's health plan.[38] These estimates reflect an initial increase in relative cost associated with quitting and a reduction in relative cost 5 years after cessation. We excluded mental health care costs incurred during the trial because our estimates lacked precision due to the extreme variance and skewness of these cost data. We considered the effect of including these estimates in sensitivity analysis. We made the simplifying assumption that survival and quality of life in former smokers is unaffected by the length of time since quitting.

All future life years, costs, and QALYs were discounted at 3% per annum. Costs were expressed in 2010 US dollars (US$). The statistical significance of the cost-effectiveness finding was determined via a Monte Carlo probabilistic

Table 2. Mean Smoking Cessation and Mental Health Services Utilization by Treatment Group During 18 Months of Follow-Up

	Experimental Group (n = 112), Mean (SD)	Control Group (n = 111), Mean (SD)
Study-provided cessation services		
Individual counseling (sessions)	0.97 (0.2)	…
NRT patch (weeks)	3.06 (3.9)	…
Computer-aided assessments (sessions)	2.20 (0.9)	…
Computer session reminders	12.43 (5.3)	…
Self-help materials	…	1.00 (0)
Out-of-study cessation services (reported)		
Individual counseling (sessions)	0.02 (0.1)	0.01 (0.1)
Group counseling (sessions)	0.01 (0.2)	0.03 (0.2)
Nicotine replacement therapy	0.30 (0.6)	0.34 (0.7)
Bupropion	0.04 (0.2)	0.02 (0.1)
Varenicline	0.04 (0.2)	0.03 (0.2)
Mental health services		
Inpatient mental health care (excluding index stay)		
Psychiatry (total days)	6.0 (14.6)	8.8 (15.7)
Psychiatry (no. of stays)	0.8* (1.3)	1.3 (1.8)
Residential addiction treatment (days)	9.6 (27.5)	6.6 (21.8)
Residential addiction treatment (stays)	0.3 (0.7)	0.2 (0.5)
Outpatient mental health care (visits)		
Emergency department visits	0.4 (0.8)	0.3 (1.3)
Day treatment/partial hospitalization	4.9 (16.4)	9.0 (32.5)
Individual visits	2.4 (6.1)	3.7 (10.9)
Subtotal outpatient mental health care	7.7 (17.3)	13.0 (34.5)
Psychiatric medication (days × no. of medications used)	414.2 (488)	467.9 (539)

*$P < .05$.
Abbreviation: NRT = nicotine replacement therapy. Symbol: … = not applicable.

sensitivity analysis, a random sampling of 1,000 sets of parameters from their estimated probability distributions. To ensure that samples were within the range appropriate to the parameter, we characterized cost using the γ distribution and quality of life using the β distribution, and constructed a probability density function from the age distribution of trial participants. The analysis accounts for uncertainty of both trial findings and the model parameters. An incremental cost-effectiveness ratio was determined from each random draw. The percentage of incremental cost-effectiveness ratios that failed to meet the criterion for cost-effectiveness represents the *P* value of the test of the statistical hypothesis that the intervention was cost-effective at a particular cost-effectiveness threshhold.[42] The model was constructed using commercially available software (TreeAge Software, Inc, 2012). For a more complete description of the model, input parameters, and sensitivity analyses, see eAppendix 1.

RESULTS

A total of 224 participants enrolled between July 2006 and December 2008, with a 79% recruitment rate. We excluded 1 participant who declined consent for medical record review. There were 112 participants in the experimental condition and 111 participants in the control condition.

Baseline Characteristics

Participants were a mean (SD) age of 39.9 (13.8) years at randomization. They had smoked a mean of 20 (13.6) years and used a mean of 19 (13) cigarettes per day. The most severe psychiatric diagnoses of study participants were schizophrenia spectrum disorders (18.9%), bipolar depression (24.3%), unipolar depression (46.8%), or another diagnosis (9.9%). An alcohol or drug problem was present in 69.4%. Most participants were men (60.4%), never married (60.2%), white (63.8%), and unemployed (54.6%); 35% had a household income < $10,000 a year. There were no significant differences in measured characteristics by treatment group assignment.

Utilization and Cost Findings

Table 2 reports smoking cessation services provided by the study and received from other sources. Experimental intervention subjects received a mean of 1 counseling session (on-unit), 2.2 computer sessions, and 3.1 weeks of NRT. Out-of-study smoking cessation services, chiefly NRT, were obtained by 25.9% of intervention participants and 25.2% of standard care participants.

The lower half of Table 2 reports utilization of mental health services during the 18 months of study follow-up. Participants randomized to the experimental intervention had significantly fewer psychiatric hospital stays, an average of 0.8 stays compared to 1.3 stays in the standard care group ($P < .05$), but the mean number of days of psychiatric hospitalization (6.0 days in the experimental group vs 8.8 days in standard care) was not significantly different. The groups had no significant differences in use of psychiatric outpatient care or medications.

Smoking cessation treatment provided by the study cost $172 for the experimental group and $22 for the control group (Table 3). When the small cost of smoking cessation services obtained outside the study was included, the total cost of smoking cessation services was $189 in the experimental group and $37 in the standard care group ($P < .001$). Randomization to the experimental condition thus added $152 in smoking cessation services cost. The bottom half of Table 3 reports the cost of mental health services received by participants after discharge from the hospitalization in which they were randomized until the end of follow-up 18 months later. There was no evidence that randomization to the experimental group increased mental health utilization. The mean cost of mental health services was $15,728 in the experimental group and $22,185 in the standard care group. Despite the large magnitude of this difference, it was not statistically significant because of great variance and the skewed distribution in costs (skewness = 3.1).

Table 4 presents trial findings used in the model. Four participants died during the study, with 2 deaths in each treatment group. Since the numbers were small, we did not use these trial events for mortality estimates in the model. Of the remaining 219 participants,

Table 3. Mean Smoking Cessation and Mental Health Cost per Participant by Treatment Group During 18 Months of Follow-Up (2010 US$)

	Experimental Group (n = 112), Mean (SD)	Control Group (n = 111), Mean (SD)
Smoking cessation services		
Study-provided smoking cessation services		
Individual counseling	$ 16 (2.7)	…
NRT patch	44 (56.3)	…
NRT mailing	1 (3.0)	…
Expert system	42 (15.0)	…
Expert system reminder	68 (29.0)	…
Provider packet mailing	1 (2.2)	…
Self-help material distribution	…	$22 (0)
Subtotal, study-provided cessation services	172 (72.8)	22 (0)
Subtotal, out-of-study cessation services	16 (33.7)	15 (31.7)
Total, smoking cessation services	189* (83.2)	37 (31.7)
Mental health services		
Inpatient mental health care		
Psychiatry (minus index stay)	$ 8,085 (19,473)	$12,202 (21,662)
Residential addiction treatment	1,418 (4,037)	963 (3,198)
Subtotal, inpatient mental health care	9,502 (20,432)	13,164 (22,501)
Outpatient mental health care		
Emergency care	107 (234)	103 (383)
Day treatment/partial hospitalization	2,838 (9,453)	5,181 (18,768)
Individual visits	1,161 (2,902)	1,398 (3,677)
Subtotal, outpatient mental health care	4,106 (9,687)	6,682 (19,089)
Psychiatric medication	2,119 (3,085)	2,338 (3,149)
Total, mental health care cost	15,728 (22,864)	22,185 (32,206)
Total, all cost	15,917 (22,871)	22,222 (32,215)

*$P < .001$.
Abbreviation: NRT = nicotine replacement therapy. Symbol: … = not applicable.

Table 4. Cost, Outcomes, and Participant Characteristics From Trial Used in Smoking Cessation Model[a]

Variable	Mean (SD)
Effectiveness of treatment (% abstinent at end of follow-up)	
Experimental intervention	18.75
Standard care	6.80
Cost of intervention during 18 mo (2010 US $)	
Abstinent at last follow-up	
Experimental intervention	240 (82)
Standard care	31 (15)
Not abstinent at last follow-up	
Experimental intervention	180 (81)
Standard care	38 (33)
Population characteristics	
Male (%)	59.9
Age (y) at follow-up	40.9 (13.64)
Utility adjustment	0.786 (0.189)

[a]Values are mean (SD) unless otherwise noted.

follow-up data were available on 199 (90.9%), including 180 followed to 18 months and 19 followed only to 12 months. We estimated abstinence among survivors at the last available follow-up at 12 or 18 months. In the experimental group, 18/96 (18.75%) were abstinent from tobacco at follow-up, compared to 7/103 (6.80%) in the control group ($P < .05$). (These figures differ slightly from the previous report,[22] which was based on individuals who completed 18 months of follow-up, who were 20% abstinent in the experimental group and 7.7% abstinent in the control group).

The incremental increase in abstinence was thus 11.95%. The short-term incremental cost-effectiveness of the experimental condition was $1,272 per quit (the incremental cost of $152 divided by the incremental effectiveness of 0.1195).

Table 4 also reports the mean cost incurred by trial participants in each treatment group contingent on abstinence status at the end of follow-up, allowing sensitivity analyses to reflect the positive correlation between cessation services cost and treatment success. Participant responses to the SF-12 resulted in a preference-based utility weight that was 0.786 of the expected value given participants' smoking status and age. We applied this value to represent the additional effect of psychiatric status on quality of life.

Cost-Effectiveness Findings

The base-case model estimated that quitting at 41 years of age results in a discounted gain of 0.83 QALYs or 1.14 life-years. The incremental cost-effectiveness of the experimental intervention determined by the model is presented in Table 5. Discounted lifetime cost with the experimental intervention was $184,057 per person, or $43 greater (95% CI, −$1558 to +$1992) than the $184,014 lifetime cost of standard care. Persons receiving the experimental intervention were expected to live 23.766 life years, or 0.139 life years more (95% CI, 0.026 to 0.250) than the 23.627 life years realized with standard care. The experimental intervention yielded 15.233 quality-adjusted life-years (QALYs), or 0.101 QALYs more (95% CI, 0.016 to 0.191) than the 15.122 QALYs realized with standard care. The additional $43 cost of experimental intervention yielded a gain of 0.101 QALYs, an incremental cost-effectiveness ratio of $428/QALY or $312/life-year.

One-way sensitivity analyses were used to test the effect of model parameters. Under the assumption that smoking cessation does not affect lifetime health care costs, (that is, if we only considered the direct cost of cessation services provided during the trial), the incremental cost-effectiveness ratio increases to $1,499/QALY. The incremental cost-effectiveness ratio remained below $5,000/QALY over a range of parameter values for relapse rate in quitters, the future quit rates of smokers, the smoking- and nonsmoking-related mortality hazard, and quality of life. Higher ratios (but still less than $10,000/QALY) were obtained if the intervention was delivered to persons 75 years of age or if smokers with psychiatric illness quality of life that was 50% of what was observed in the trial.

A probabilistic sensitivity analysis was used to test the significance of the cost-effectiveness finding. Using a threshold of $50,000/QALY as the criteria for cost-effectiveness, the hypothesis that the intervention was cost-effective was significant with $P = .01$ (that is, 99.0% of the replicates were cost-effective at this threshold).

Had the model included the short-term mental health care costs observed during the trial, the experimental intervention would have saved $6,414 relative to the control condition, that is, the intervention would have strongly

Table 5. Cost, Outcomes, and Cost-Effectiveness From Lifetime Markov Model

Strategy	Experimental Intervention	Standard Care	Difference
Cost (2010 US $)			
Cost of cessation treatment in trial	189	37	152
Discounted cost of follow-up health services	183,868	183,977	−109
Total discounted cost	184,057	184,014	43
Outcomes			
Discounted life-years	23.766	23.627	0.139
Discounted quality-adjusted life years	15.233	15.122	0.101
Incremental cost-effectiveness ratio			
Dollars/life-year		312	
Dollars/quality-adjusted life-year		428	

dominated standard care, as it was cost-saving and more effective. A probabilistic sensitivity analysis with these costs included found that the intervention was not significantly cost-effective at any threshold criteria. This result is attributable to the great variance and skewness in the mental health costs observed during trial follow-up.

DISCUSSION

This randomized clinical trial determined that an intervention for smokers initiated during a smoke-free psychiatric hospital stay and continued 6-months after hospitalization was cost-effective relative to standard care.

The short-term incremental cost-effectiveness of the intervention was $1,272 per quit. This was better than the mean incremental cost effectiveness of $2,777 per quit found in a systematic review of 14 smoking cessation studies[18] (expressed in 2010 dollars).

We estimated that an individual with the psychiatric illness of trial participants who quits smoking at 41 years of age will realize a discounted gain of 0.83 QALYs or 1.14 life-years. This benefit is lower than the typical value of 2 QALYs per quit benefit estimated for other smokers,[15,43–46] reflecting the higher nonsmoking mortality hazard and lower health-related quality of life associated with psychiatric illnesses. Although we estimated the benefit per quit to be to be lower in this population than in smokers generally, the intervention was still highly cost-effective.

The incremental cost-effectiveness ratio of $428/QALY was lower (more cost-effective) than smoking interventions in other populations. Brief physician advice has an incremental cost-effectiveness ratio of $1,240–$3,620/QALY (in 2010 US$).[43] Addition of pharmacotherapies to counseling has an incremental cost-effectiveness of $1,133–$1,774/QALY.[16] Varenicline for prevention of relapse in recent quitters has an incremental cost-effectiveness of $3,413/QALY.[47] Like other smoking-cessation interventions, this intervention was highly efficient, yielding additional QALYs for a cost that was well below the commonly used threshold for judging cost-effectiveness (the range of $50,000–$100,000/QALY in the United States).

There was no evidence that the intervention increased the utilization or cost of mental health services. The experimental group incurred a mean of $15,728 mental health service cost, compared to $22,185 in the standard care group, a difference that was not statistically significant. Our previous trial of smoking cessation for psychiatric outpatients with depression had this same result, with a nonsignificant trend toward lower mental health services costs in the group assigned to receive more intensive cessation services.[48] Concern has been expressed that smoking cessation treatments may worsen outcomes in psychiatric patients.[49] This study added to the evidence that treating smokers identified in psychiatric settings does not increase mental health care cost.

We acknowledge several limitations. In the absence of adequate information, we assumed that relapse rates in former smokers are 150% higher in persons with mental illness than in the general population. We used quit rates for continuing smokers as are observed in the general population. Our findings were robust across a wide range of relapse and spontaneous quit rates, however. In the absence of better information, we assumed that the effect of smoking cessation on health care cost is unaffected by the presence of a psychiatric illness. The trial lacked the statistical power needed to estimate the effect on smoking-cessation mental health costs.

The burdens of smoking on persons with mental illness and substance use disorders have been cited as reasons why these groups should be given priority in tobacco control efforts.[50] We found that cessation treatment for smokers identified during a psychiatric hospitalization was as cost-effective as cessation services provided to tobacco users without mental illness, as determined by other studies. This suggests that there will not necessarily be any loss of efficiency if tobacco control efforts prioritize services for persons with mental illness.

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Supplementary material: See eAppendix 1 in the accompanying pages.

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Supplementary material follows this article.

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Supplementary Material

Article Title: Cost-Effectiveness of Smoking Cessation Treatment Initiated During Psychiatric Hospitalization: Analysis From a Randomized, Controlled Trial

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List of Supplementary Material for the article

1. eAppendix 1 Description of model, input parameters, and sensitivity analyses

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This Supplementary Material has been provided by the author(s) as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

Supplementary appendix to
"Cost effectiveness of Smoking Cessation Treatment Initiated during Psychiatric Hospitalization"

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1. Model Overview

We evaluated the cost-effectiveness of a smoking cessation intervention for smokers identified during a psychiatric inpatient stay relative to standard treatment . The costs of the smoking cessation intervention were incurred during the time horizon of the trial, but most of its benefit comes from avoided cardiovascular disease and cancer. These benefits will not be realized until many years later. This supplementary appendix provides detailed information on the Markov model that we constructed to project the costs, life years and quality-adjusted life years (QALYs) of participants using a life time horizon.

We developed a simple model with two non-absorbing states: smoker and former smoker (see Figure 1). The model was initially populated according to the smoking status of participants in each treatment group at the end of trial follow-up and evaluated the lifetime cost and outcomes in each group.

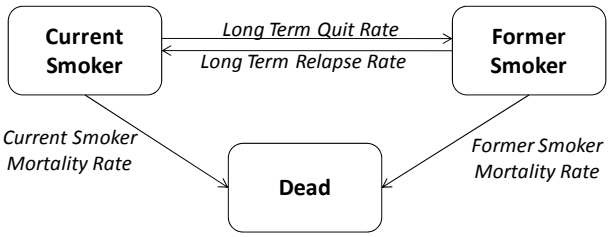

Figure 1 Lifetime Markov Model

Each individual entered the model as either a current smoker or a former smoker. A current smoker may quit and a former smoker may relapse and become a current smoker at any time during their remaining life. Death may occur in either state. Transitions between states were calculated in 3 month intervals. All future life years, costs and QALYs were discounted at 3% per annum.[1, 2] Costs were expressed in 2010 US dollars. The model was constructed using commercially available software (TreeAge 2009). The parameters used in the base-case model, the results of the base-case model, and the results of sensitivity analyses are described below.

2. Model Parameters Obtained from the Trial

Model parameters obtained from trial data are listed in Table 1, including information about the standard deviation of estimates and the distribution used to characterize uncertainty for the probabilistic sensitivity analysis.

We represented outcomes according to the smoking status reported by trial participants at their last follow-up visit. Cost includes the cost of all smoking cessation services used during the trial. Costs were determined separately by randomization assignment and smoking status at the end of the trial follow-up period. This specification linked smoking cessation service cost with outcomes, so that sensitivity analyses reflect the positive correlation between cost of cessation services and probability of treatment success.

Table 1: Model Parameters obtained from the trial

Variable	Base Case	SD	Distribution
Effectiveness of treatment (% abstinent at end of follow-up)			
Experimental Intervention	18.75	-	Beta
Standard care	6.80	-	Beta
Cost of Intervention (2010 $ U.S.)			
Sustained Abstinence			
Experimental Intervention	239.92	82.01	Gamma
Standard care	31.29	15.17	Gamma
No Sustained Abstinence			
Experimental Intervention	179.96	81.15	Gamma
Standard care	37.79	32.53	Gamma
Population characteristics			
Male (percent)	59.91	-	Beta
Age at follow-up (years)	40.87	13.64	Probability density table
Utility relative to utility for general population of same age, gender, and smoking status	.786	.189	Beta

A follow-up smoking status assessment was available at the 18 or 12 month follow-up for 199/219 trial participants (90.9%) who survived to the end of the trial. Deaths (n=4) were balanced by treatment group. Among those randomized to the experimental intervention, 18/96 (18.75%) were abstinent from tobacco use at follow-up. Among those randomized to standard care, 7/103 (6.80%) were abstinent. (These figures differ slightly from the previous report, based on observations of individuals who completed 18 months of follow-up, who had 20% abstinence in the experimental group and 7.7% abstinence in the control group).[3]

The mean age of participants at follow-up was 40.87, and ranged from 19 -76 years (SD 13.64 years). We characterized the age distribution of trial participants by creating a probability density function. We determined the proportion of individuals who were in groups defined by 5

year age ranges, and the mean age in each range (Table 2). We sampled from this probability density table for probabilistic sensitivity analysis.

Table 2. Probability density function for age at randomization

Age range	Frequency	Mean age at randomization
< 20	0.040	18.9
20-24	0.126	22.5
25-29	0.135	26.7
30-34	0.090	31.7
35-39	0.126	37.0
40-44	0.094	42.1
45-49	0.090	47.0
50-54	0.135	51.5
55-59	0.090	56.9
60-64	0.031	61.4
65-69	0.031	66.4
70-74	0.004	72.0
75-79	0.009	75.0

The health related quality of life of study participants was assessed using the SF-12. We used the method of Brazier to score this as patient utility.[4] We used this information to incorporate into the model a parameter that reflects that the utility of trial participants was lower than the utility in the population.

We compared the patient utility at the end of trial follow-up to the average population utility given smoking status and age category (see Section 6). We estimated the effect of non-smoking factors, including mental illness, on quality of life, by dividing the utility of the final assessment of each participant by the utility in a population of primary care patients matched by age and smoking status. The utility adjustment in Table 1 represents the mean value of this ratio.

3. Model Parameters from the Literature- Transition between Smoking States

The model required information on the rate at which persons who are smokers at the beginning of one period quit and are found to be non-smokers at the beginning of the following period, as well as the rate at which former smokers relapse and become current smokers.

Quit Rates Among Current Smokers. Many quit attempts are of very short duration and result in rapid relapse. Since the benefits of quitting on health are likely to be realized only if quitting is sustained, we defined "former smoker" as someone who had quit at least one year. We used a 4.3% annual rate quit rate.[5, 6] Our probabilistic sensitivity analysis used the distribution implied by a 95% confidence interval covered by the range of 3% to 5.6% observed in several different studies.[7-10]

Relapse Rates Among Former Smokers. Long-term studies of former smokers show that relapse rates are high shortly after quitting, and that the longer a quit attempt is sustained, the less likely relapse will occur. Our review of the literature found a 15% annual relapse rate in the first year after a one-year sustained quit (that is, the second year after quitting)[11] and diminishing rates for subsequent years.[11-14] The time dependent change in the probability of relapse was modeled as a series of tunnel sates. The former smoker who completed a period without relapse proceeded to the next tunnel state with a diminished probability of relapse.

Table 3. Annual relapse rate after one year of abstinence

Time frame after initial quit	Annual relapse rate among former smokers	Low	High	Source
Year 2	15%	2%	23%	[11, 14]
Year 3-5	5%	1.3%	8.2%	[12, 13]
Year 6-9	2%	1.3%	2.5%	[11, 12]
Year 10	1%	0.5%	2.5%	[11, 14]

Table 3 reports relapse rates from published sources regarding smokers observed in the general population. Since persons with psychiatric illness have higher smoking prevalence, we assumed that those with the psychiatric illnesses observed in this trial were 150% as likely to relapse as the general population, and multiplied all rates in Table 3 by 150%.

4. Model Parameters from the Literature- Mortality Hazard from Smoking

We estimated age and gender specific mortality rates for smokers and formers smokers. We started with the gender specific age-adjusted mortality rates for U.S. residents who were never smokers. These rates were adjusted to reflect the additional risk of mortality associated with smoking status. We used age-specific estimates of the excess mortality hazard associated with smoking. These estimates were developed from a review of the literature.[15-25] The excess mortality associated with smoking was represented as the excess hazard associated with being a current or former smoker, relative to the population of never smokers. We estimated separate excess hazards for age brackets of 24-54 years, 55-74 years, and 75 years and older (see Table 3). [15-18, 20, 24-26]

Table 4: Excess Mortality Associated with Smoking Status Relative to Never Smokers

Cohort	Base Case	Low	High	Source
Female				
24 – 54				
Current Smoker	1.369	1.261	1.701	17, 18, 20, 24
Former Smoker	1.214	1	1.441	18, 20, 24
55 – 74				
Current Smoker	2.533	2.365	2.865	17, 18, 20, 24
Former Smoker	1.666	1.308	1.893	18, 20, 24
75+				
Current Smoker	1.411	1.353	1.685	17, 18, 20, 24
Former Smoker	1.111	1	1.337	18, 20, 24
Male				
24 – 54				
Current Smoker	2.486	2.017	2.932	17, 18, 20, 24
Former Smoker	1.074	1	1.10	18, 20, 24
55 – 74				
Current Smoker	2.550	1.967	2.995	17, 18, 20, 24
Former Smoker	1.992	1.866	2.177	18, 20, 24
75+				
Current Smoker	1.326	1	1.771	17, 18, 20, 24
Former Smoker	1.074	1	1.10	18, 20, 24

5. Model Parameters from the Literature- Mortality Hazard of Mental Illness from Causes Other Than Smoking

Persons with mental illness have high smoking prevalence and high mortality rates. The additional mortality hazard is not solely due to smoking related disease, however, and includes mortality hazard from other substance use problems, accident, suicide, and other non-smoking related illness.

In order to estimate the long-term impact of smoking cessation on survival in this population, we needed information on the mortality risk associated with mental illness from causes other than smoking. We need to consider this extra risk so that our model did not underestimate mortality risks, and potentially overestimate the benefit from smoking cessation.

Estimation of this parameter is complicated by the different mental illnesses of trial participants. We estimated the extra risk for schizophrenia and depression, and used a weighted average of these risks.

We estimated the average mortality hazard in trial participants from causes other than smoking to be 1.43. For sensitivity analysis, we assumes the range of values spans the interval of 1.28 - 1.59 in a triangular distribution.

Mental illness of trial participants. The psychiatric illnesses of study participants were assigned hierarchically, so that participants were characterized by their most severe condition. The conditions of participants included schizophrenia spectrum disorders (18.9%), bipolar depression (24.3%), unipolar depression (46.8%), and other (9.9%).

Excess mortality in schizophrenia from causes other than smoking. To estimate the mortality risk from causes other than smoking, we combined the age-adjusted mortality hazard ratio in schizophrenia with information about the extra mortality hazard from smoking in schizophrenia.

The mortality hazard in schizophrenia can be regarded as the product of a non-smoking mortality hazard ratio and the smoking mortality hazard ratio:

$$HR_{\text{all cause}} = HR_{\text{smoking}} * HR_{\text{non-smoking}}$$

Three studies examined the extra mortality hazard from smoking in persons with schizophrenia. A long-term follow-up study of persons hospitalized for schizophrenia found the age-adjusted mortality hazard was 2.1 times greater in smokers than in non-smokers in this cohort [27]. Follow-up of a smaller cohort of patients with schizophrenia found after 13 years, the standardized mortality rate in smokers was 2.2 times that of non-smokers,[28] and after 25 years, 1.95 times that of non-smokers.[29]

This information can be used to calculate the mortality risk from smoking in patients with schizophrenia. Kelly found that 55% of patients with schizophrenia were smokers and that their age-adjusted mortality hazard was 2.1 times that of non-smokers.[27] The smoking risk is thus the average of the mortality hazard of smokers (2.1) and non-smokers (1.0), weighted by the prevalence of smoking (55%) and non-smoking (45%). The smoking related hazard is thus 1.65 (i.e. [2.1*55%] + [1.0*45%]).

A meta-analysis found that persons with schizophrenia had an all-cause Standardized Mortality Rate of 2.5.[30] This pooled estimate considers the effect size and sample size of the individual studies. Earlier meta-analyses had found lower mortality rates.[31, 32] The newer estimate used data from 18 studies published after 1995, an important difference because the relative mortality hazard associated with this illness has been increasing.

We estimate a non-smoking mortality hazard in schizophrenia of 1.56. This was the all-cause hazard ratio divided by the smoking hazard ratio, that is, 2.5 (from Saha's meta-analysis [30]) divided by 1.605 (the weighted average of Kelly's study comparing risks of smokers to non-smokers[27]).

Excess mortality in bipolar disorder from causes other than smoking. We found no comparable information to estimate mortality from non-smoking causes in persons with bipolar disorder. Smoking prevalence and all-cause mortality associated with bipolar disorder are high and similar to the rates observed for schizophrenia. The now outdated meta-analysis of mortality risks in mental illness reported a Standardized Mortality Rate of 202 for bipolar disorder, compared to an SMR of 157 in schizophrenia.[32] Smoking prevalence in bipolar disorder is also quite high, and similar to that of schizophrenia. The most recent data found smoking prevalence was 46.4% in bipolar disorder and 59.1% in schizophrenia.[33] Because of these similarities, and in the absence

of alternative information, we applied our estimate of non-smoking mortality hazard in schizophrenia to represent the risk in patients with bipolar disorder.

Excess mortality in depression from causes other than smoking. We used information on the mortality risk in depression that controlled for smoking status. Individuals with depression had 1.32 times the relative mortality risk of persons without depression, controlling for age and health behaviors, including smoking status.[34]

Weighted average non-smoking mortality hazard. We estimated the average mortality hazard in trial participants from causes other than smoking to be 1.43. This is a weighted average of the estimate for persons with schizophrenia and for those with unipolar depression. The weights were determined by the prevalence of disease in trial participants. 43.2% of trial participants had diagnosis of schizophrenia or bipolar disorder, and 46.8% had unipolar depression. We ignored the 9.9% participants who did not have any of these three conditions in weighting these estimates, arriving at weights of 52% depression and 48% schizophrenia or bipolar disorder. The estimate of 1.43 reflects that weighted average of non-smoking mortality hazard for depression (1.32 * 52%) and schizophrenia (1.56*48%).

Uncertainty of estimates. We estimated the range of the mortality hazard from causes other than smoking for sensitivity analysis. For schizophrenia, we estimated that the confidence interval for smoking related mortality was plus or minus 12%, based on the fact that the difference between minimum and maximum values (1.95 – 2.2) reported in the two studies by Brown was 25% of the value at the middle of their range. This results in a range of hazard ratios from 1.37 – 1.74. For depression, we used the confidence interval reported by Kinder, 1.20 – 1.45. Using the disease prevalence rates to weight the upper and lower bounds of these estimates results in a range of hazard ratios of 1.28 – 1.59.

6. Model Parameters from the Literature- Quality of Life

Cost-effectiveness analysis requires information on the Quality Adjusted Life Years, with years survival adjusted by a preference-rated health related quality of life, also called utility. Smokers and former smokers have a quality of life that is less than that of persons with perfect health; quality of life also diminishes with age.[35-39] Studies of the effect of smoking status have been conducted in the U.S. population but did not distinguish former smokers from never smokers.[36, 39]

We included the effect of smoking on quality of life in our model by using the mean preference based quality of life estimated by smoking status, gender, and age, in a survey of preference based qualify of life in the English population.[37] These are reported in Table 5. These estimates include the effect of smoking associated with smoking related chronic disease.

Table 5. Preference-based health related quality of life by smoking status, age, and gender

Age	Former Regular Smokers		Moderate Smokers	
	Mean	SE	Mean	SE
Men				
16-24	0.9342	0.0054	0.9211	0.0065
25-34	0.9306	0.0047	0.9166	0.0062
35-54	0.9058	0.0041	0.8899	0.0060
45-54	0.8596	0.0042	0.8422	0.0063
55-64	0.8020	0.0050	0.7815	0.0070
65-74	0.7802	0.0059	0.7575	0.0079
75-100	0.7358	0.0059	0.7112	0.0082
Women				
16-24	0.9084	0.0053	0.8952	0.0065
25-34	0.8988	0.0045	0.8835	0.0061
35-54	0.8872	0.0041	0.8716	0.0060
45-54	0.8479	0.0041	0.8317	0.0062
55-64	0.7827	0.0051	0.7648	0.0070
65-74	0.7709	0.0057	0.7520	0.0076
75-100	0.6987	0.0067	0.6778	0.0087

These values were adjusted by the quality of life estimates of trial participants, in order to reflect the additional impact of mental illness on quality of life. We calculated utility for trial participants relative to the utility for the general population of same age, gender, and smoking status.

We used a beta distribution to characterize the preference estimates in Table 5 and to characterize the adjustment to preference adjustment to trial data. Sampling from these distributions for the probabilistic sensitivity analysis limited utility estimates to a range with a lower limit of zero and an upper limit of one.

7. Model Parameters from the Literature- Health Care Cost

Smoking cessation leads to improvement in health that may result in the use fewer health care services, reducing cost. Most models of the cost-effectiveness of smoking cessation interventions have, however, ignored the effect of quitting on health care cost.[40, 41]

Existing literature on the effect of smoking cessation on cost is largely based on models. These models estimate the impact of smoking on the development of smoking related disease the result effect on cost. There is mixed evidence whether quitting actually reduces life time health care cost. Several papers have found that although health costs are lowered by the lower morbidity in quitters, they are offset by at least as much by the additional cost resulting from extended length of life.

There are a few long-term follow-up studies of cost incurred after participation in a smoking cessation clinical trial. These studies have found that quitting was associated with greater health care costs in the short term, but that in subsequent years, health care costs were lower in sustained quitters than in continuing smokers.[42-44]

We used data from a large study of health care claims to determine the effect of smoking status on health care charges relative to the entire population, and applied these estimates to age and gender specific health care cost from the U.S. Medical Expenditure Panel Survey.

An evaluation of claims data by Musich et al from persons under 65 in an employer health plan found annual health care charges in persons over 4 years after self-reported smoking status. [45] The analysis controlled for age and gender. Current smokers and former smokers who quit fewer than 5 years previously incurred significantly higher charges than never smokers. Persons who had quit 5-9 years previously had higher charges than never smokers if they had one of three specified chronic diseases; but charges were not higher in those that did not have one of these chronic diseases. This analysis reported p values, but not standard errors. The estimates from this study have been used as model parameters in other studies.[46, 47]

We used data from Musich to determine the excess cost association with smoking status relative to the entire population. We calculated ratios for current smokers, recent quitters (less than 5 years), and long-term quitters (5 years or more) relative to the entire population. Musich reported mean charges and frequencies for groups defined by smoking status and chronic disease status. We found the frequency weighted mean charge of all individuals in each smoking status group, and expressed these as a ratio (Table 6). Musich reported p values for comparisons of current smokers and recent quitters to non-smokers, for subgroups defined by chronic illness. We calculated standard errors using Z score associated with those tests for each chronic illness group. [49] We found the frequency weighted mean of these standard errors. There was insufficient data to estimate the pooled variance. Musich did not compare costs of current smokers (or recent quitters) to long-term former smokers. We note that the costs of long-term former smokers were not significantly different from the cost of never smokers, and used the same standard errors relative to never smokers as the estimate of standard errors relative to long-term former smokers.

Table 6. Health care charges incurred by smokers and former smokers relative to the general population

	Mean of ratio	SE
Smokers	1.1881	.0934
Recent quitters (< 5 years)	1.2476	.1014
Long-term quitters (5+ years)	0.9595	Reference

We obtained data from the Medical Care Expenditures Panel Survey (MEPS) on the total health care expenditures by gender and age group (Table 7).[48] The model used the health care expenditure appropriate to the age in each model cycle, adjusted for the ratio given smoking status in that period. Expenditures were assumed to be gamma distributed for probabilistic sensitivity analysis.

Table 7. Total health care expenditures per U.S. resident, 2010, by gender and age category

Age	Mean	SE
Female		
18-24	2,235	224.73
25-44	3,347	127.80
45-64	6,229	291.38
65-90	9,623	394.82
Male		
18-24	1,072	111.75
25-44	2,158	248.56
45-64	5,217	258.40
65-90	10,249	483.08

8. Model Calibration

The model was calibrated to remaining life expectancy as derived in Brønnum-Hansen and Juel from a large Danish study.[50] To establish its validity in a US population, we also compared remaining life expectancy in the absence of an intervention to that calculated by BENESCO's natural history model[51] and Sloan's life table of an average smoker.[26] These calibrations were done without the additional mortality hazard from non-smoking causes in serious mental illness.

Projected benefits of quitting. At the mean age for the base case, 40.9 years, a person entering the model as a former smoker had a discounted life-expectancy of 24.685 additional years (or 15.8940 discounted QALYs). Those entering the model as a current smoker had a discounted life-expectancy of 23.548 additional life years (or 15.0644 discounted QALYs). The model thus projected that the benefit of quitting was 1.137 discounted life years or 0.8303 discounted QALYs.

Compared to other models, this model projected fewer benefits of smoking cessation. This reflects the increased mortality hazard utility and lower utility in persons with psychiatric illness compared to persons of the same age and smoking status in the general population. Fiscella and Franks estimated the benefit of quitting to be between 0.69 to 2.38 discounted QALYs with less gain among those who were older at the time they quit.[52] They reported a mean benefit of 1.98 QALY per quit. Cromwell reported a mean benefit of 1.97 discounted QALY per quit.[53] Chirikos found the benefit to be 2.2 QALYs per successful quit.[54] Javitz estimated the benefit from quitting to be 2.6 discounted life years.[55] Godfrey estimated the benefit as 3.6 discounted life years.[56]

9. Results

The results of the base case model are presented in Table 8. Discounted life time cost with the experimental intervention was $184,057, or $43 more than the $184,014 lifetime cost of standard care.

Persons receiving the experimental intervention were expected to live 23.766 life years, or 0.139 life years more than those the 23.627 life years realized with standard care. Experimental intervention yielded 15.223 quality adjusted life years (QALYs), or 0.101 QALYs more than the 15.122 QALYs realized with standard care.

The additional $43 cost of experimental intervention yielded a gain of 0.101 QALYs, an incremental cost-effectiveness ratio (ICER) of $428 / QALY or $312 / LY.

Table 8. Lifetime Cost-Effectiveness Model-- Base Case Results

Strategy	Experimental Intervention	Standard Care	Difference
Cost			
Cost of cessation treatment in trial	189	37	152
Discounted cost of follow-up health services	183,868	183,976	-108
Total discounted cost	184,057	184,014	43
Outcomes			
Discounted Life Years	23.766	23.627	0.139
Discounted Quality Adjusted Life Years	15.233	15.122	0.101
Incremental Cost-Effectiveness Ratio (ICER)			
$/LY	$312/LY		
$/QALY	$428/QALY		

10. One-Way Sensitivity Analyses

Cost. We considered the effect of including only the cost of the smoking cessation intervention, that is, of assuming that smoking cessation had no effect on the cost of subsequent health care services. With this assumption, the cost of the experimental intervention was $152 and the corresponding ICER under this assumption was $1,499/QALY.

Other parameters. One-way sensitivity analyses were performed on all model parameters derived from trial data identified in (Table 9). The entry “Experimental Dominant” in the table indicates that the Experimental Group incurred fewer costs and enjoyed better outcomes than the control group.

Table 9. One Way Sensitivity Analysis of Other Model Parameters

Variable	Value	ICER ($/QALY)	ICER ($/LY)
Age (years)	18	Dominant	Dominant
Age (years)	75	13,041	8,610-
Male (percent)	80	1,944	1,403
Male (percent)	50	Experimental Dominant	Experimental Dominant
Utility adjustment	1	336	312
Utility adjustment	0.40	850	312
High effectiveness of experimental intervention (percent abstinent)	25%	Experimental Dominant	Experimental Dominant
Low effectiveness of experimental intervention (percent abstinent)	12%	2,468	1,803
High effectiveness of control intervention (percent abstinent)	14%	2,542	1,844
High effectiveness of control intervention (percent abstinent)	2%	Experimental Dominant	Experimental Dominant
High cost of experimental intervention (% of baseline cost)	150%	1,371	1,002
Low cost of experimental intervention (% of baseline cost)	50%	Experimental Dominant	Experimental Dominant
High cost of standard care (% of baseline cost)	150%	243	178
Low cost of standard care (% of baseline cost)	50%	612	447
Low long-term natural cessation rate in current smokers	3% per year	669	486
High long-term natural cessation rate in current smokers	5.6% per year	224	164
Low relapse rate in former smokers (% of base case rates)	50%	Experimental Dominant	Experimental Dominant
High relapse rate in former smokers (% of base case rates)	150%	2,670	1,973
Inclusion of mental health care cost incurred during trial (percent included)	100%	Experimental Dominant	Experimental Dominant

11. Probabilistic Sensitivity Analysis

Probabilistic Sensitivity Analysis (PSA) was conducted using the fitted probability distribution from trial data and the literature. The discount rate employed the range of values suggested in guidelines for conducting cost-effectiveness analysis.[1, 2]

Table 10 provides the confidence intervals determined by each strategy for cost, life years, and quality adjusted life years, and the confidence interval for the point estimates of the differences between strategies in cost, life years, and quality adjusted life years.

Table 10. Confidence Intervals of Cost and Outcomes from Probabilistic Sensitivity Analysis

Strategy	Median	Lower Bound of 95% Confidence Interval	Upper Bound of 95% Confidence Interval
Discounted Cost			
Experimental Intervention	181,896	128,224	211,143
Standard Care	181,539	126,657	211,653
Difference (Δ)	122	-1158	1992
Discounted Life Years			
Experimental Intervention	25,223	8.707	38.215
Standard Care	25.080	8.644	38.110
Difference (Δ)	0.122	0.026	0.250
Discounted Quality Adjusted Life Years			
Experimental Intervention	14.0897	4.1541	29.9076
Standard Care	14.0021	4.1000	29.8095
Difference (Δ)	0.088	0.016	0.191

Each replicate from the probabilistic sensitivity analysis was used to generate an incremental cost-effectiveness ratio. The plot of these point estimates is given in Figure 2.

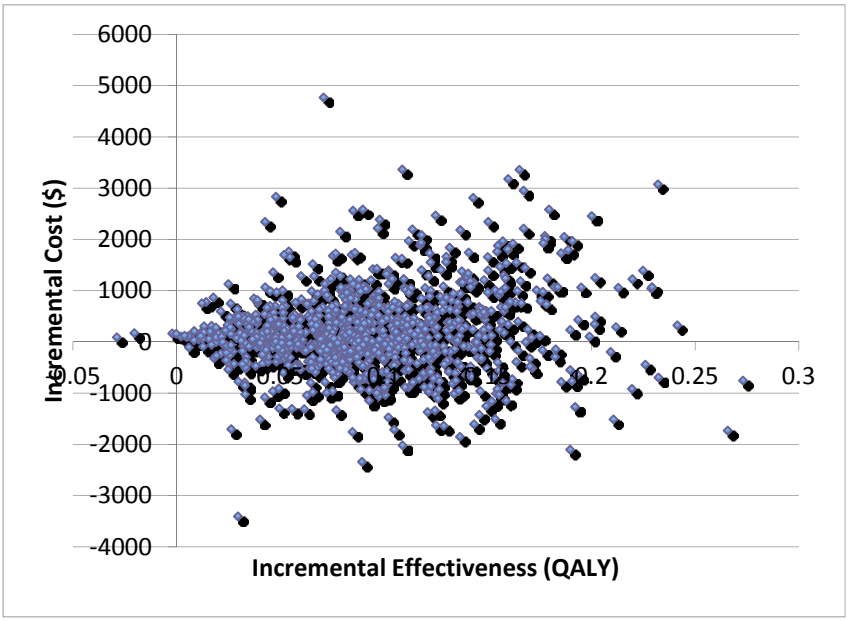

Figure 2: Plot of Incremental Cost and Incremental Effectiveness form Probabilistic Sensitivity Analysis

The cost-effectiveness acceptability curve represents tests of the statistical significance of cost-effectiveness at different thresholds used to assess cost effectiveness.[57] Figure 3 plots the probability that the intervention was cost-effective at thresholds up to $100,000 per QALY. A probability of greater than 0.95 represents a finding that the intervention was found to be significantly cost-effective with the probability of less than 0.05 of a Type I statistical error. At the conventional willingness to pay threshold of $50,000 / QALY, the experimental intervention was 0.99 likely to be cost-effective, with the probability of a Type statistical error value of 0.01.

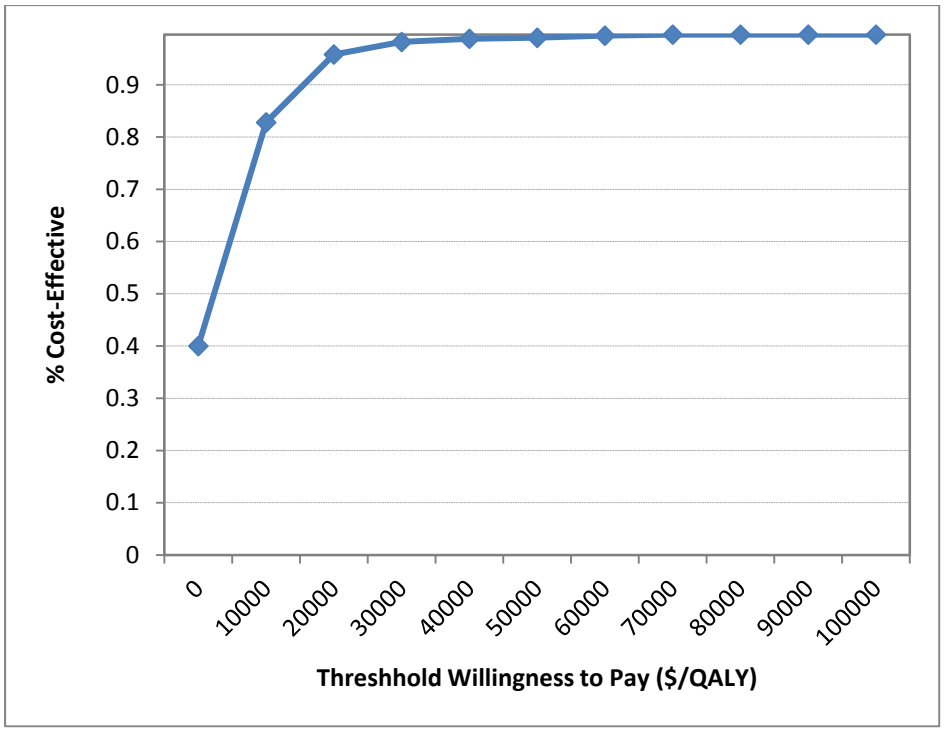

Figure 3: Cost-Effectiveness Acceptability Curve

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