# Cost-Effectiveness of a Smoking Cessation Program Implemented at the Time of Surgery for Lung Cancer

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**Background:** Many patients are active smokers at the time of a diagnosis of surgically resectable lung cancer. Perioperative smoking cessation is associated with improved survival, but the cost-effectiveness of a smoking cessation program initiated immediately before surgery is unknown.

**Methods:** We developed a decision analytic Markov model to evaluate the incremental cost-effectiveness of a formal smoking cessation program. The parameter estimates were taken from the available literature. The model included the cost and effectiveness of the smoking cessation program, cost and incidence of perioperative complications, postoperative mortality, and utility measured in quality adjusted life years (QALY). Dollars per QALY and life year were calculated and one-way sensitivity analyses were performed.

**Results:** The cost/QALY and cost/life year were $16,415 and $45,629 at 1 year after surgery and $2609 and $2703 at 5 years, respectively. Most sensitivity analyses showed the 1 year postsurgery cost/QALY estimates were less than $50,000, and all were less than $12,000 at 5 years. Cost-effectiveness estimates were most sensitive to the frequency of perioperative complications and the estimated short-term utility estimates.

**Conclusion:** A smoking cessation program initiated before surgical lung resection is cost-effective at both 1 and 5 years postsurgery. Providers should encourage patients who are still smoking to engage in formal smoking cessation programs.

**Key Words:** Cost-effectiveness, QALY, Smoking cessation program, Non-small cell lung cancer.

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Lung cancer is the second most common cancer among men and women in the United States and the leading cause of cancer-related mortality[1] with 90% of all lung cancer diagnoses attributable to smoking tobacco.[2] Smoking cessation decreases the risk of lung cancer[3] and interventions to induce abstinence have been found to reduce lung cancer incidence and mortality.[4,5] In addition, smoking cessation programs are cost-effective by most standards; for example, a study of the Agency for Health Care Policy and Research smoking cessation program guidelines showed an incremental cost-effectiveness of $1915 per quality adjusted life year (QALY) at 1 year after the intervention.[6]

Approximately 20% of patients actively smoke at the time of lung cancer surgery and 30 to 60% of these patients continue to smoke afterward.[7,8] Cessation shortly before surgery for lung cancer is associated with improved long-term survival.[9] Discussing or receiving a diagnosis of a smoking-related illness is not associated with abstinence.[10] However, lung cancer surgery may be a "teachable moment" and cessation programs at the time of surgery for patients without lung cancer are effective.[11–15] Limited evidence suggests smoking cessation programs may be effective for patients with lung cancer[16,17] and are recommended.[18]

Expected 5-year survival for non-small cell lung cancer (NSCLC) is 60 to 75% for stage I and 36 to 60% for stage II disease.[1] This survival time is likely long enough for patients to enjoy quality of life improvements from abstinence.[19] No study has evaluated a smoking cessation intervention for patients referred for surgical management of lung cancer.[20] We used the available evidence to develop a decision analysis model to evaluate the cost-effectiveness of a smoking cessation intervention initiated preoperatively for patients with NSCLC.

## PATIENTS AND METHODS

We developed a decision analytic Markov model to evaluate the incremental cost-effectiveness of a smoking cessation program initiated before surgical resection for patients with NSCLC at stage IIIB or less compared with patients not offered a program (usual care). The decision tree, describing perioperative outcomes and 1-year survival, is shown (Figure 1) with probabilities, utility, and costs of the model in Table 1. We included costs from the perspective of health care providers. The model was analyzed in Microsoft Excel SP2003 (Redmond, WA).

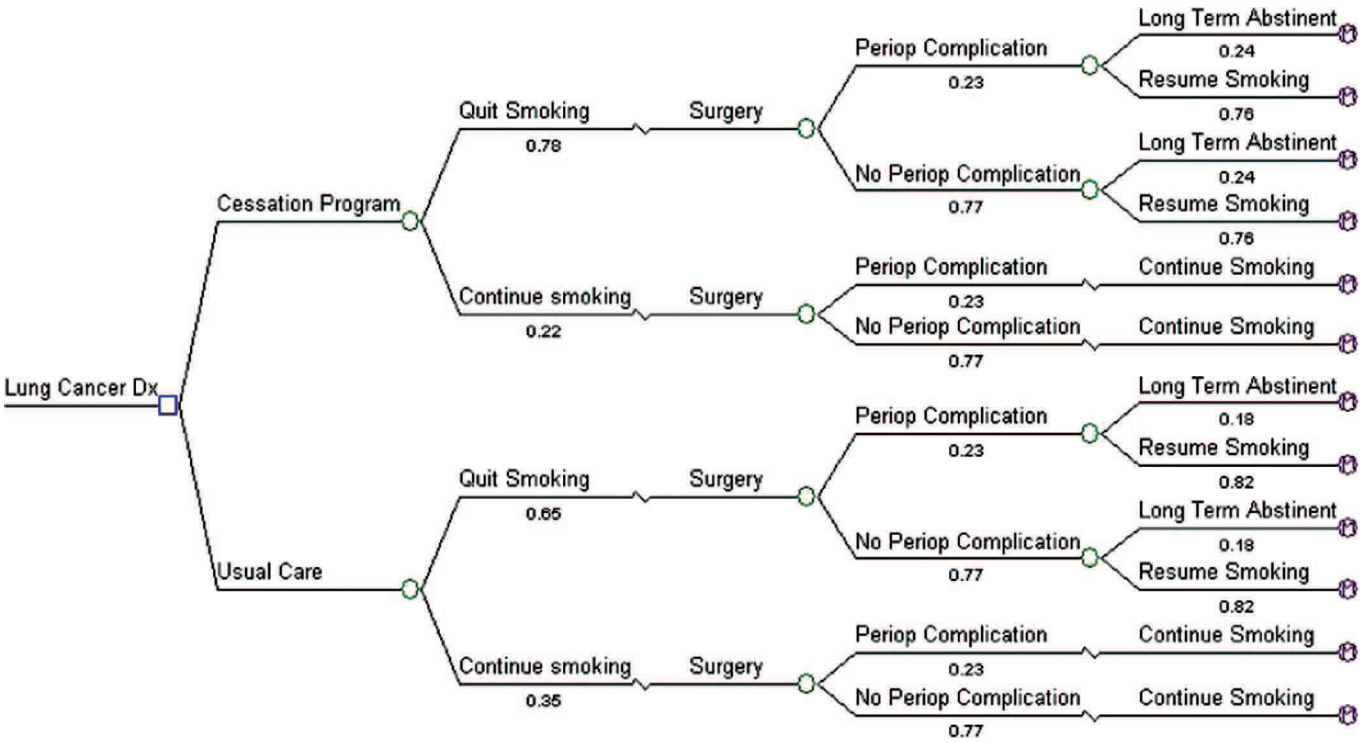


**FIGURE 1.** It shows the decision tree developed from the available evidence. Patients diagnosed with resectable stage IIIB or less non-small cell lung cancer are offered a smoking cessation program or usual care. Each number represents the probability of progressing to one stage or the other. Periop, perioperative.

## Effectiveness of Smoking Cessation Program

Preoperative smoking cessation programs have been studied in heterogeneous settings[11–14] so an overall effectiveness estimate is not available[15]. We used an estimate based on a similar setting to ours, using a program of counseling and nicotine replacement.[11] Seventy-eight percent of smokers in the treatment arm were abstinent at the time of surgery compared with 65% of usual care patients; 3 months postsurgery, the abstinence rate was 19% compared with 12% of patients in usual care. Long-term abstinence likely underlies some of the mechanism for improved survival for those who quit before surgery[21] and provides a more conservative estimate in this case. Thus, we chose these latter parameters for estimating long-term mortality but use the rates at the time of surgery for the perioperative complication estimates. All studies showed an improvement in abstinence rates with a formal program so a 5 percentage point improvement was used as the minimal difference for the sensitivity analysis.

## Cost of Smoking Cessation Program

The program includes nicotine replacement with two short (Centers for Medicare & Medicaid Services [CMS] Current Procedural Terminology code 99401) and two long (99402) sessions; average reimbursement is $13 and $25 for codes 99401 and 99402, respectively.[22,23] We test program costs in a sensitivity analysis that include costs of bupropion or varenicline therapy.[24]

## Perioperative Pulmonary Complications Probabilities

Most studies have not shown a differential rate of perioperative complications.[11,12,25,26] Recent quitters (<2 months of abstinence) and current smokers both had a 23% incidence of perioperative complications after thoracotomy for lung cancer.[26] An oft-quoted study found 33% of current smokers had perioperative pulmonary complications compared with 57% for recent quitters (<8 weeks of abstinence).[27] Thus, we used a 23% rate of complications for both groups in the primary analysis, increasing the complication rate up to 40 percentage points higher for recent quitters in a sensitivity analysis.

## Perioperative Pulmonary Complication Costs

CMS does not pay for complications after lobectomy or pneumonectomy except when the case becomes a cost outlier.[28] However, perioperative pulmonary complications are associated with a 73% increase in direct costs,[29] leading to an estimated total cost of $30,896 based on average CMS reimbursement.[30]

## Mortality

Current smokers at the time of resection for NSCLC of stage IIIB or less had a median survival of 43 months.[9] In comparison, 77% of recent quitters (3 months to 1 week before surgery) were alive at 5 years. The sensitivity analysis reflects the upper 95% confidence interval for the smallest

**TABLE 1.** Parameter Estimates

| Parameter | Base Case (Range) | References |
|---|---|---|
| Smoking cessation program costs | | |
| Cost per visit | | 19, 20 |
| 99401 (G0375) | $13 | |
| 99402 (G0376) | $25 | |
| Nicotine patches (8 wk supply) | $123.96 | 21 |
| Total | $199.96 ($50–$450)[a] | |
| Smoking cessation program effectiveness | | |
| Program abstinence rate 3 mo postsurgery[b] | 19% (12–62%) | 11 |
| Usual care abstinence rate 3 mo postsurgery[b] | 12% | 11 |
| Program abstinence rate at time of surgery[c] | 78% | 11 |
| Usual care abstinence rate at time of surgery[c] | 65% | 11 |
| Perioperative complications | | |
| Recent quitters | 23% (23–63%) | 23, 24 |
| Current smokers | 23% | 23, 24 |
| Surgical costs | | |
| No complications | $17,859 | 27 |
| Perioperative pulmonary complications | $30,896 | 26 |
| Yearly mortality | | |
| Recent quitters | 5.1% | 9 |
| Current smokers | 17.6% (10–55%) | 9 |
| Utility scores | | |
| Recent quitters | 0.64 (0.47–0.99) | 8, 28, 29 |
| Current smokers | 0.49 | 8, 28, 29 |

[a] Range includes cost of bupropion or varenicline.
[b] Used for mortality estimates of program compared with usual care participants.
[c] Used for perioperative complication estimates of program compared with usual care participants.

difference in mortality rates between continued smokers and recent quitters.[9]

## Health-Related Quality of Life

The mean health-related quality of life (HRQOL) utility score postsurgery is 0.59 for patients with operable NSCLC.[31] Thirty-two percent were current smokers, but the utility score was not stratified by smoking status. Therefore, we used a second study of lung cancer survivors to approximate utility scores by smoking status although we could not directly convert the HRQOL score to a QALY.[8] The score was 28.7 for current smokers compared with 22.1 for former smokers. In our base case analysis, we used this crude 77% (22.1/28.7) adjustment to the utility score (0.59), and the proportion of smokers and nonsmokers, to estimate utility scores for current smokers (0.49) and recent quitters (0.64).

Recent quitters may have decreased HRQOL early after cessation[32] although this difference is reversed at 1 year.[19] We use 1-year utility gains from quitting in our base case but use a short-term decreased QALY for quitters (based on converting SF-36 scores to QALYs[33]) in sensitivity analyses.

**TABLE 2.** Markov Transition Probabilities (yr 2–5)

| | End of Year | | |
|---|---|---|---|
| Start of Year | Smoker | Nonsmoker | Dead |
| Smoker | 0.824 | 0 | 0.176 |
| Nonsmoker | 0 | 0.949 | 0.051 |
| Dead | 0 | 0 | 1 |

## Markov Analysis

Three states after resection were possible: alive smokers, alive nonsmokers, or dead. To convert 5-year mortality rates[9] to annual transition probabilities ($tp_1$) between states for the Markov model we used the formula: $tp_1 = 1 - (1 - tp_5)^{1/5}$. The annual probability of mortality for recent quitters and current smokers is 5.1% and 17.6%, respectively (Table 2). We assumed that any deaths during a year occurred on average half way through the year (i.e., half cycle correction) and used a discount rate of 3% per year for outcomes after the first year.

## Sensitivity Analyses

One-way sensitivity analyses of cost-effectiveness at 1 and 5 years postsurgery were performed for the postoperative complication rate, the cost of the intervention, effectiveness of the intervention, mortality difference between current smokers and recent quitters, and difference in utility scores (Table 1). We use a cost per QALY of $50,000 as a threshold value.[34]

# RESULTS

One year after surgery the smoking cessation program group had 0.48 QALYs compared with 0.47 QALYs for the usual treatment group (Table 3). Subjects assigned to a smoking cessation program had 0.924 life years compared with 0.920 life years for the group in usual care. These differences equate to a cost/QALY of $16,415 and a cost/life year of $45,629. The Markov analysis shows that the cumulative life years and QALYs continue to separate over time (Table 3). For example, there was a difference of 0.09 QALYs and 0.08 life years at 5 years postsurgery. These differences equate to a cost/QALY of $2609 and a cost/life year of $2703.

If perioperative complications occur at a differential rate of 33% for continued smokers and 57% for recent quitters (as in Warner et al.[27]), the cost/QALY was $49,945 and the cost/life year was $138,835 at 1 year postsurgery. At 5 years, these estimates yielded a cost/QALY of $7938 and a cost/life year of $8224. Figure 2 shows how cost/QALY and cost/life year at 5 years postsurgery is affected as the differential perioperative complication rate in subjects who are recent quitters increases. At 1-year postsurgery, the threshold value (cost/QALY of $50,000) occurred if recent quitters had a differential rate of perioperative complications 24 percentage points higher than smokers, with no threshold at 5 years.

**TABLE 3.** Markov Analysis for Cumulative QALY's and Life Years and Costs Effectiveness by Year After Surgery

| | Program | | Usual Care | | | |
|---|---|---|---|---|---|---|
| Year[a] | QALYs | Life Years | QALYs | Life Years | Cost/QALY[b] | Cost/life Year[b] |
| 1 | 0.48 | 0.924 | 0.47 | 0.920 | $16,415 | $45,629 |
| 2 | 0.89 | 1.71 | 0.87 | 1.69 | $7,441 | $12,455 |
| 3 | 1.25 | 2.38 | 1.20 | 2.34 | $4,649 | $6,120 |
| 4 | 1.55 | 2.95 | 1.49 | 2.89 | $3,344 | $3,813 |
| 5 | 1.82 | 3.44 | 1.73 | 3.36 | $2,609 | $2,703 |

[a] Utilizes half cycle correction.
[b] Includes 3% discount/yr.
QALY, quality adjusted life years.

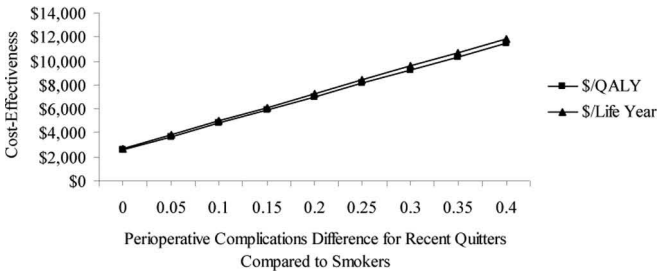


**FIGURE 2.** It shows the 5-year postsurgery differences in cost/quality adjusted life years (QALY) and cost/life year as the proportion of recent quitters who suffer perioperative complications increases over the rate of continued smokers with perioperative complications. Note that the base case assumes no difference in the proportions suffering perioperative complications.

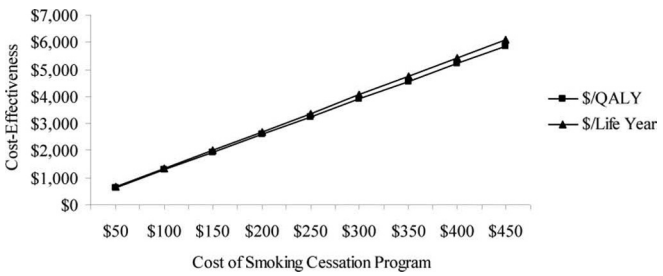


**FIGURE 3.** It shows the 5-year postsurgery differences in cost/quality adjusted life years (QALY) and cost/life year as the cost of the smoking cessation program changes. Note that the base case has a cost of approximately $200.

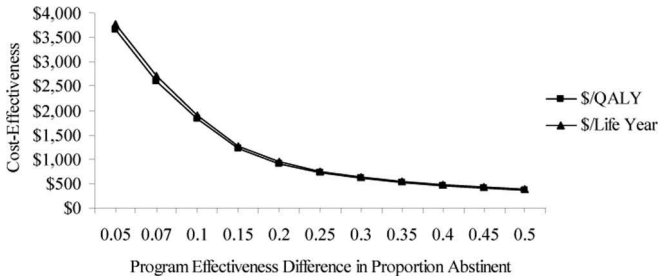


**FIGURE 4.** It shows the 5-year postsurgery differences in cost/quality adjusted life years (QALY) and cost/life year as the effectiveness of the smoking cessation program changes. Note that the base case assumes the smoking cessation program leads to an increase of 7% of the subjects achieving abstinence at 3 months postsurgery.

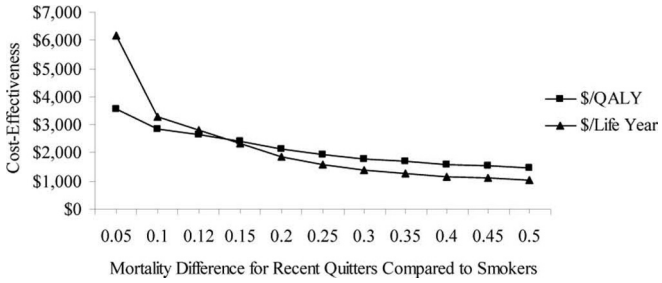


**FIGURE 5.** It shows the 5-year postsurgery differences in cost/quality adjusted life years (QALY) and cost/life year as the proportion of smokers who are deceased at 1 year after surgery increases over the proportion of recent quitters who are deceased. Note that the base case assumes that smokers have a 12% higher proportion who are deceased at 1 year compared with recent quitters.

At the upper limit of $450 for the smoking cessation program, the cost/QALY and cost/life year at 5 years postintervention were $5871 and $6083, respectively (Figure 3). At both 1 and 5 years postsurgery, the threshold value of cost-effectiveness was not reached.

At 1 year assuming an increase of 5 percentage points for smokers achieving abstinence at 3 months with the program, the cost/QALY and cost/life year were $22,981 and $63,881, respectively. At 5 years, these estimates are $3652 and $3784, respectively. Figure 4 shows how cost-effectiveness changes as the effectiveness of the program at inducing abstinence at 3 months postsurgery increases over usual care. At both 1 and 5 years postsurgery, the threshold value of cost-effectiveness was not reached.

At 1 year postsurgery with a 5 percentage point increased mortality for continued smokers compared with recent quitters, that is, a mortality rate of 10.1% for continued smokers, the cost/QALY, and cost/life year were $18,368 and $114,263 respectively. At 5 years postsurgery, this differential rate of mortality translated to a cost/QALY of $3560 and

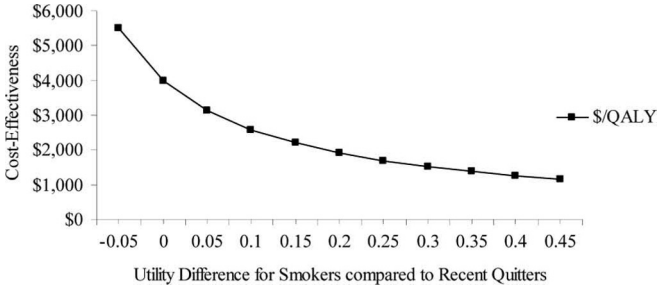


**FIGURE 6.** It shows the 5-year postsurgery differences in cost/quality adjusted life years (QALY) as the utility of smokers changes with respect to quitters. Note that the base case assumes that quitters have a utility score 0.15 higher than smokers.

a cost/life year of $6182 with the ranges shown in Figure 5. At both 1 and 5 years postsurgery, the threshold value of cost-effectiveness was not reached.

At 1 year postsurgery if recent quitters had a utility estimate of 0.02 less than smokers, the program was associated with a cost/QALY of $252,567. At 5 years postsurgery, this lower utility adjustment for quitters had a cost/QALY of $6467 with the ranges shown in Figure 6. At 1 year postsurgery the cost-effectiveness occurred at a threshold of quitters having a utility score 0.03 higher than smokers and did not occur for any estimate of utility at 5 years postsurgery.

## DISCUSSION

Cost-effectiveness of a smoking cessation intervention at 5 years after surgery was estimated to be $2609 per QALY and was less than $12,000 per QALY under most assumptions tested in the sensitivity analyses. These estimates are sensitive to changes in the differential rate of perioperative pulmonary complications based on smoking status. Five years after surgery, the one-way sensitivity analyses of the cost of the program, effectiveness of the program, mortality difference between continued smokers and recent quitters, and utility difference between smokers and quitters are all consistent with cost-effectiveness estimates of less than $7000 per QALY and life year. In comparison, it has been estimated to cost $47,676 per QALY to pursue annual computed tomography surveillance for recurrence after resection for stage IA NSCLC.[35]

Many patients actively smoke at the time of a diagnosis of lung cancer[7] and there may be pessimism by both patients and clinicians regarding the value of abstinence. However, tobacco cessation even at this late stage is associated with both decreased mortality and increased quality of life.[8,9] Our results indicate that at 5 years after surgery, the cost-effectiveness of a smoking cessation program is likely below the commonly used threshold of $50,000/QALY.[36] The results 1 year after surgery are similar although more affected by the utility and perioperative complication estimates.

Cost-effectiveness analyses using decision analytic models developed from the available evidence are limited by the availability, quality, and generalizability of data to inform the model. Several studies have explored the prognostic value of preoperative smoking status with mortality after lung cancer resection.[37–40] Only one observational study evaluates the association of short-term preoperative smoking cessation on subsequent mortality, and this study did not evaluate stage-specific survival.[9] However, there was no stage and smoking status interaction observed in this analysis so the overall difference in mortality is likely the same for recent quitters and continued smokers with the same stage of disease. Smoking status at the time of chemotherapy is associated with its effectiveness,[21] but no data are available on postoperative recidivism rates to guide inclusion of this aspect in the model. The sensitivity analysis of mortality differences for smokers and recent quitters shows that a smoking cessation program is likely cost-effective even with minimal differences in mortality.

The QALY estimates are limited by the available evidence. The only study that examined the differences in utility associated with smoking status in lung cancer survivors used a measure that cannot be translated into a QALY.[8] Smoking cessation is associated with increased utility at 1 year[19] at the expense of a decrease in short-term utility,[32] and it is unclear when this decrement is reversed. Thus, our results may overestimate cost-effectiveness for patients who die shortly after surgery. In addition, quality of life is affected by stage of disease[31] but there was no information how this differs by smoking status. However, if quitters have a better quality of life than current smokers regardless of stage, our results are still applicable. Overall, the sensitivity analysis shows a program is likely cost-effective over a broad range of utility estimates.

Our Markov analysis examined three postoperative states, alive-smoker, alive-nonsmoker, or dead, but there are certainly gradations of quality of life. It may be that recent quitters have fewer recurrences, in which case our analysis is conservative. Alternatively, those who would have died had they not quit, might have a poor quality of life if they develop metastases and other complications.

We did not include costs of treating recurrent or metastatic disease. The lower mortality in recent quitters[9] might be due to lower rates of recurrence and metastases. A smoking cessation program would probably be more cost-effective once the costs of treating these disease stages are included. However, if recent quitters are less likely to die, but live longer with recurrent or metastatic disease, we would overestimate the cost-effectiveness of the cessation program. We did not include costs and effects of treating other smoking-related diseases which presumably would decrease the cost/QALY.

Despite the conflicting data on the timing of smoking cessation and perioperative pulmonary complications, there is no evidence of increased mortality for recent quitters.[25–27] Perioperative complications lower quality of life, but there are no data to guide estimates of utility. In addition, because our utility estimates are derived from cohorts of patients who likely suffered perioperative complications, our results incorporate short-term quality of life decrements. However, similar to our overall estimate of QALYs, our results overestimate the cost-effectiveness for patients who survive a short period of time after surgery.

Our results are not applicable to lung cancer patients with inoperable disease. The results may be less relevant to patients who are expected to survive a short time after surgery although even the 1-year cost-effectiveness estimates are below $50,000 per QALY. Individual patients may be able to quit smoking without assistance so a formal cessation program may not offer incremental benefit.

Smoking cessation is beneficial in most situations, even for those who have already been diagnosed with operable lung cancer. Our results show a smoking cessation program is likely to be cost-effective over a broad range of underlying assumptions about mortality, utility, and program effectiveness. We suggest that smokers undergoing evaluation for lung cancer should participate in smoking cessation programs and health care payers cover the expenses.

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