Tobacco Use Screening and Counseling: Technical Report Prepared for the National Commission on Prevention Priorities

Version 06.1; last updated May 11, 2006

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This work was supported by the Centers for Disease Control and Prevention (CDC) and the Agency for Healthcare Research and Quality (AHRQ).

A. USPSTF Recommendation, November 2003

The USPSTF strongly recommends that clinicians screen all adults for tobacco use and provide tobacco cessation interventions for those who use tobacco products *(A Recommendation)*[1] The USPSTF found good evidence that brief smoking cessation interventions, including screening, brief behavioral counseling (less than 3 minutes), and pharmacotherapy delivered in primary care settings, are effective in increasing the proportion of smokers who successfully quit smoking and remain abstinent after 1 year.

B. Choice of Interventions to Study

In accordance with the recommendation, we focused our literature review and estimates on randomized controlled trials of interventions that could be conducted in a busy primary care practice on most of their tobacco-using patients and that were tested under conditions consistent with those criteria. Such interventions can be delivered repeatedly over multiple years to be consistent with cancer screening services and immunizations delivered as a series of vaccines. Our goal was to produce one estimate of CPB and CE that reflects the proportion of individuals counseled who would and would not utilize cessation medications. To do this, we first separately assessed the literature on feasible office counseling and the literature on cessation medication prescription (since all medication trials also include some degree of counseling). We did not strictly follow the USPSTF guideline of 3 minutes, since many studies did not report the time necessary for intervention and that would have eliminated many good trials of interventions that were also clearly feasible in the practices where they were conducted. However, studies of more intensive counseling or of interventions that involved many counseling/reinforcement contacts as a part of follow-up after the original intervention were eliminated as efficacy studies infeasible in practice. The complication in this, as in the USPSTF recommendation itself, was that all the studies are based on the effects of one or a few contacts over a brief period of time. Unfortunately, there are no studies of what really happens in primary care practice – repeated brief interventions during many contacts for a variety of medical reasons. Finally, while the recommendation uses the term tobacco, the evidence comments, like the vast majority of the literature, addresses cigarette smoking, not other forms of tobacco use. Therefore our estimates of CPB and CE were also limited to cigarette smoking.

C. Literature Search and Abstraction

C1. Effectiveness Literature:

The literature examining tobacco cessation is considerable. To most efficiently identify key studies on smoking cessation interventions, we started our search with the extensive meta-analyses performed by Fiore et al. as part of the creation of the Public Health Service clinical guideline on Treating Tobacco Use and Dependence published in 2000.[2] Fiore et al used 163 articles in their 23 meta-analyses, which included literature published through the end of 1998. In order to identify studies published since Fiore's meta-analyses, we conducted Level 1 and Level 2 literature searches[3] for clinical trials which identified an additional 595 articles from PubMed published between January 1999 and April 2004. We also conducted Level 1 and Level 2 literature searches[3] looking specifically for observational studies; this search yielded 505 articles from PubMed. As a result of these searches and review of references in identified articles, we identified a total of 255 articles for potential abstraction.

In order for an article to be abstracted, it had to have a control/comparison group, follow-up of at least one year, 50 or more subjects per intervention arm, analyze smoking cessation as an outcome, and may have an intervention that was feasible in a busy primary care practice. This reduced the 255 articles identified to a total of 23 articles for abstraction for estimating effectiveness.[4-26]

During the adjudication process, 6 of these articles were found to have various issues that made them unusable for our purposes, so these articles were eliminated. In the Lancaster study, all participants were offered brief advice from their physician prior to random assignment, creating no true control group.[23] This intervention was also too intense for primary care. Hughes also had an intervention that was too intense for primary care and was excluded.[7] Yudkin's study had a very low response rate, making any conclusions of dubious value.[21] The intervention in the Aveyard study was carried out by research staff, and few participated in the intervention or returned the questionnaire.[11] The Killen study was really a study of relapse prevention.[13] Finally, OXCHECK was excluded as some people were included in the analysis of both the control and intervention groups.[22] We were left with 17 articles for the analysis of the effectiveness of tobacco cessation.

<u>C2. Cost Effectiveness Literature:</u>

We performed Level 1 and Level 2 literature searches[3] for cost effectiveness articles from January 1, 1992 through March 30, 2005, which identified 1,252 articles. Among these articles and others identified in the bibliographies of obtained articles, we identified 68 original articles on the costs of smoking or the cost-effectiveness of smoking cessation interventions for adults. Eight of these were cost-effectiveness studies with results reported as cost per quit,[27-34] and an additional 27 were cost-effectiveness studies with results reported as cost per life year saved or quality adjusted life year saved.[35-61] Among the latter subset, 14 studies reported either the CE of brief to moderate intensity advice by primary care clinicians or the CE of smoking cessation aids.[37;40-43;45;48-50;52;54;55;59;61] None of the studies reported the CE of repeated interventions delivered over multiple years. Therefore we did not abstract any articles and instead we developed a CE estimate based upon our CPB calculation.

D. Clinically Preventive Burden (CPB) Estimate

CPB is the population burden addressed by the service multiplied by the effectiveness of the service if all smokers received the service repeatedly over their lifetimes. Table 1 shows the summary calculations for CPB. The data points in Table 1 are either estimates from the literature or are calculated based upon other data in the table. The *Base Case* column shows the point estimate for each variable used in our calculation of CPB or the result of a calculation. For data points taken from the literature, the *Data Source* column in Table 1 shows the reference numbers on which the estimate is based. For data points that are calculated within the table, the *Data Source* column shows the calculation formula. The letters in the formula refer to the row labels in the left most column for the data points on which the calculation is made. The *Range* column shows the range over which the point estimates are varied in our sensitivity analysis. We created additional tables (not shown) to summarize the evidence and perform supporting calculations. In the following text, we describe relevant content from these tables.

<u>D1. Gains in Life Expectancy:</u>

<u>Ever-smokers: Row a.</u>

The number of ever-smokers in birth cohorts has declined over-time. This trend explains part of the differences in ever-smokers across age groups in the current population, and makes it difficult to use the available data on cross-sections to estimate the proportion of individuals in the cohort now becoming adults who will be ever-smokers. For our base-case, we use the portion of ever-smokers in the current 35-44 year-old age group (45.1%).[62] This percentage is applied to the 98.8% of a birth cohort of 4,000,000 who survive to age 18.[63] Our range of ever-smokers in sensitivity analysis is based on the portion of ever-smokers in the 24-35 (40.2%) and 45-55 (51/6%) year-old age groups.[62] Because our estimate of the effectiveness of repeated counseling (Section D2 and Appendix) reflects the portion of ever-smokers who would quit as a result of repeated counseling, we use ever-smokers in a birth cohort in estimating the burden of smoking rather using the prevalence of smoking at a point in time.

<u>Average Gains in Life Expectancy (LE) from Quitting: Row b.</u>

Rogers et al. estimated LE for never, current, and former smokers, using the National Health Interview Survey and National Mortality Feedback Survey.[64] Differences between former and current smokers provided a measure of the increase in life expectancy that can be obtained by quitting, although there is no control for other risk factors. An additional problem in using the difference in LE to estimate the benefits of cessation was that some former smokers are likely to have quit due to smoking attributable illnesses. This may cause us to underestimate the benefits of quitting as a result of counseling.

Taylor et al. used observed smoking status in 1982 and follow-up data on mortality through 1996 in a prospective study of 1.2 million U.S. residents to estimate the gains in life-expectancy from smoking cessation.[65] However, Taylor et al. categorized former smokers who quit within the last 3 years as current smokers to overcome the problem of former smokers who quit as the result of severe smoking attributable illness.

In both studies, the results were reported by age and gender. We calculate a weighted average from these stratified results using the age distribution of persons in the 2003 BRFSS who reported having stopped smoking for at least one day in an attempt to quit. Ideally, this average would be calculated using the age distribution of long-term successful quits that occurs after repeated counseling, but no such data are available. Using the age distribution of quit attempts, the average increase in life expectancy from quitting, using the data provided by Rogers et al., is 4.71 and the corresponding average for the data provided in Taylor et al. is 6.59. The estimate based upon Rogers et al. may be conservative due to inclusion of former smokers who quit as a result of smoking-attributable illness. On the other hand, the estimate based upon Taylor may be too high due to the exclusion of all former smokers who quit within the last 3 years. Therefore, we use the average of these estimates (5.65) in estimating CPB (row b). We excluded from this average four other studies reporting LE for current and formers smokers due to their reporting only for limited age groups,[66] limiting health benefits to coronary heart disease,[67;68] and inadequately reporting results for former smokers.[69]

<u>D2. Gains in Quality of Life:</u>

<u>QALYs Lost Due to Smoking-attributable (SA) Morbidity: Row c.</u>

Table 2 provides the detail for this calculation, and the total is entered in row c of Table 1. For most conditions, we calculate the lifetime number of SA cases as the number of years of life lived by a birth cohort of 4 million after the age of 35 years multiplied by the SA fraction of the annual incidence of disease. For example, among adults 35 years of age and older, the annual incidence of oral cancer is 21.0 per 100,000. From life tables,[63] we estimate that there would be 164,596,352 years of life lived after the age of 35 in a birth cohort of 4 million. An estimated

64.6% of oral cancers are attributable to smoking.[70] Thus, approximately 164,596,352 × 0.00021 × 0.646 = 22,325 cases of SA oral cancers are predicted to occur over the lifetime of a birth cohort of 4 million. Cases for pediatric diseases and fire injuries are calculated using the number of years of life lived from birth rather than age 35.

Smoking attributable QALYs lost to morbidity are the product of the lifetime incidence of SA disease, the duration of disease, and the associated quality of life reduction (QALY weight). Continuing the example using the data in Table 2 for oral cancers, 4.3 x 0.2 = 0.86 QALYs are lost to morbidity for each case, and a total of 22,325 x 0.44 = 19,200 QALYs are lost to smoking attributable oral cancers over the lifetime of the birth cohort.

The annual incidence rate for the morbidity calculations in Table 2 comes from several sources. Cancer cases are based on 2001 incidence rates, age-adjusted to the 2000 population (unadjusted rates were not reported).[71] For most other conditions, 2001 hospital stays with the ICD-9 of interest listed as the primary diagnosis arre used when available.[72] The exceptions are:

- Congestive heart failure – using lifetime incidence[73]
- Strokes - using the annual incidence of first strokes[74]
- Pneumonia and influenza – using self-reported medically-attended episodes[75]
- Bronchitis, emphysema, and COPD – using the incidence of COPD from the Global Burden of Disease study[76]
- Fire injuries – using the cases of injuries from home fires[77]

With the exception of fire injuries, the disease categories listed in Table 2 are those for which SA mortality is reported in SAMMEC.[70] We apply the mortality SA fractions (SAFs) from SAMMEC to morbidity because SAFs for cases of disease are not available for most SA diseases.

The duration of illness for many conditions (all cancers, stroke, congestive heart failure, chronic airways obstruction) are from closely corresponding (i.e., not always identical) disease categories of the Global Burden of Disease estimates for Established Market Economies.[76] Incidence data on many chronic conditions are not available. When necessary, we use the incidence of hospital stays and we treat the morbidity calculation as an estimate of the quality of life lost due to acute episodes of chronic disease. For each hospital stay we assign a three-week duration of illness to reflect both the hospital stay itself and subsequent recovery time. Longer durations are assigned for hospital episodes of childhood disease cases and shorter durations to medically treated cases of influenza and pneumonia.

Estimates of the QALYs lost per year lived with an illness (QALY weight in Table 2) are the standard ranges used in this study of 0.3 for acute conditions and 0.2 for chronic conditions.[3;78] Cancers of less than two-year duration are treated as acute illnesses because of their low survival rates. However, QALYs lost per year for stroke of .40 (range .25 to .55) is based on published estimates from utility scales rather than the standard QALY weight for chronic conditions because the utility scales indicate that strokes have substantially higher quality of life losses per year than most other chronic conditions.[79-85]

<u>QALYs Lost to SA Illnesses: Row d-g.</u>

The total QALYs attributable to smoking are divided by the number of ever-smokers (row a) to obtain an estimate of morbidity-related QALYs lost per ever-smoker (row d). However, QALYs lost per ever-smoker understate the burden for lifelong smokers because this group includes former smokers. Therefore, rows e through g provide a correction for this problem by estimating the morbidity QALYs lost for current smokers using the equation shown for row g. This formula is derived algebraically from the following equations:

i. SA QALYs per ever-smoker = (SA QALYs per former smoker × % of former smokers) + (SA QALYs lost per current smoker × % of current smokers)
ii. SA QALYs lost per former smokers = SA QALYs lost per current smoker × relative risk of SA disease of former smokers compared to current smokers

The relative risk of all SA diseases for current smokers compared to former smokers is not known. However, the relative risk of SA mortality and SA expenditures can be calculated from existing literature. If smokers have the same case fatality rates as former smokers, the relative risk for disease should be similar to the relative risk of mortality. And if smokers have the same costs per case as former smokers, the relative risk of diseases should be similar to their relative expenditures on SA disease. It is not clear whether one of these relative risks is a better approximation of the relative risk of disease than the other. Therefore, we use the average of these two measures.

The relative risk of SA expenditures is calculated from one study that reported total charges for current, former, and never-smokers over 4 years according to smoking status.[86] By comparing current smokers to former smokers who had quit for 5 or more years, we estimate the relative cost of SA charges to be 0.535 after 5 years as a former smoker. We use estimates for those who had quit for 5 or more years in order to exclude former smokers who had quit following illness.

We computed the relative risk of mortality from three studies that used different data sources: the American Cancer Society, CPS II study;[65] the National Center for Health Statistics surveys;[87] and a prospective observational study of British doctors.[88] In order to calculate relative mortality risk, we limited studies to those that reported the mortality risk for current, former and never-smokers. The average relative mortality risk calculated from these three studies is 0.249 (range 0.20 to 0.30). The average of the relative SA expenditures and the relative risk of SA mortality is 0.39 (row f). This average is used as an estimate of the relative risk of SA disease in the calculation of QALYs lost from SA morbidity per continuing smoker (row g). In sensitivity analysis we vary this estimate from the lowest estimate from the mortality studies (0.20) to a higher estimate of relative SA expenditures (0.56) that is calculated by the average of relative expenditures of three studies in addition to Musich et al. that were not used for the base case estimate due to important limitations.[89-91] The per-quitter morbidity reduction is the difference between current and former smokers in morbidity-related SA QALYs as calculated for row h (0.353 QALYs in the base case).

<u>Short Term (1 Year) Effectiveness of Primary Care Interventions: Row i.</u>

As noted above in Section B, we limited our estimate to those interventions that were feasible in busy primary care practices. We included both brief and medium (but not intensive) interventions in the counseling estimate and separately estimated a quit rate for counseling plus medication. We found 12 good trials of brief/medium interventions without smoking cessation aids,[5;6;9;12;15-20;24;25] and 6 with such aids in primary care settings.[4;8;10;14;15;26] These studies produce estimates of 2.4% and 5.0% respectively, with the same 2:1 advantage for cessation medication use found in many trials in a variety of settings.

<u>Marginal Long-term Effectiveness of Repeated Counseling: Row j</u>.

Our search did not identify any estimates of the long-term effectiveness of brief to medium counseling with or without medications that was delivered repeatedly over multiple years. Since this is the situation in usual practice we felt it necessary to develop our own estimate of the effectiveness of repeated counseling. Furthermore, our estimates of CPB and CE for tobacco cessation counseling in our ranking of clinical preventive services had to reflect repeated delivery to provide valid comparisons with other services in the ranking such as cancers screenings that are also delivered at regular intervals. Two studies of very intensive counseling repeated over 3-6 years observed a quit rate of 23%[92] and 25%,[93] with additional reductions in smoking among the intervention group participants who smoked at baseline compared to the usual care participants who smoked at baseline. Several aspects of these studies make their results unsuitable for use in our estimate of CPB - both studied counseling that is too intensive to be practically carried out in primary care, and study subjects were volunteers at high risk for heart disease. Both studies were carried out in the mid-1970s and suggested that their 3-6 year intervention and observation periods may be inadequate to quantify the benefit of repeated intervention because differences between intervention and control group were diminishing substantially at the end of the study periods.

Therefore, in order to estimate the effectiveness of long-term repeated counseling, we built a sub-model that answers the question of “What marginal long-term quit rate with repeated advice is consistent with the trend in counseling delivery rates, the trend in total quits among smokers, the trend in quits that are not prompted by clinician advice (spontaneous quits), as well as with the 12-month marginal quit rates estimated from the literature as summarized above (2.4% without smoking cessation aids, and 5.0% with the use of smoking cessation aids)”. The appendix describes this model and the data inputs to the model in detail. The results of the sub-model indicate long-term marginal effectiveness of repeated counseling is 20% without the use of smoking cessation aids and 38% for the portion of those counseled who choose to use smoking cessation aids in their quit attempt. Weighting these two estimates with the sub-models estimate of the portion of those counseled who choose to use a smoking cessation aid in 2003 (16%), the estimated average long-term effectiveness of repeated counseling is 23.1% (row j).

As discussed in the appendix, the sub-model is highly sensitive to several key data inputs, and therefore we chose several base-case estimates for the sub-model that produce a more conservative estimate of long-term effectiveness of repeated counseling. We also use a wide range of estimates for long-term effectiveness in sensitivity analysis of CPB and CE. We use the one-year marginal quit rates (2.4% and 5.0%) weighted as above (2.8%) as our low estimate of long-term effectiveness. This estimate implies that, at a minimum, repeated counseling will add enough additional quitters in subsequent years to replace those who relapse after quitting for the initial 12 months. We limit our high estimate to three times the base case estimate (69.3%), the sensitivity of the sub-model shows that virtually any estimate up to 100% effectiveness is mathematically possible.

Base Case Estimate of CPB: Row k.

Our base case estimate of CPB is 2,474,00 QALYs saved (row k), which is calculated as the sum of the mortality and morbidity gains in quality adjusted life years per smoker counseled, multiplied by the number of ever-smokers counseled in a birth cohort of 4,000,000 individuals, and the long-term effectiveness of repeated counseling.

D3. Sensitivity Analysis for CPB:

Because years of life gained with counseling far exceed health years of life equivalents from reduced illness, any variables that are specific to estimating quality of life gains have little influence on the estimate of CPB. For example, even if systematic error in our estimate of QALYs lost to illness caused us to underestimate this number by 50%, it changes CPB by less than 3%. In contrast, CPB is moderately sensitive to changes of the years of life years saved by cessation and highly sensitive to changes of the long-term effectiveness of repeated advice. When we change these three variables simultaneously, we derive an extremely wide CPB range of 231,000 to 9,170,000 QALYs saved. This wide range is not as problematic to our ranking as it may first appear because even the lower bound estimate places tobacco cessation counseling among the services with the highest CPB.

E. Cost Effectiveness (CE) Estimate

We produced a CE estimate based upon the health benefits estimate for CPB, because no published estimates of the CE of counseling delivered repeatedly over multiple years are available. This estimate is outlined in Table 3, which builds on data points and calculated variables in Table 1. Thus, the row lettering of Table 1 is continued in Table 3. We estimate the cost-effectiveness of screening by adding service costs, cost-savings, and discounting to the estimate of CPB. We estimate CE over the recommended over the lifetime of ever-smokers in a birth cohort of 4,000,000. We follow our methods for producing consistent estimates of CE across preventives services.[3;94] These methods are consistent with the ‘reference case’ of the Panel on Cost-Effectiveness in Health and Medicine.[95] The methods include use of a 3% discount rate for both costs and health benefits, the exclusion of productivity losses from disease costs, and the exclusion of medical costs that are not related the conditions prevented by the service. We use year 2000 dollars for all cost data.

<u>E1. Cost of Counseling</u>

<u>Cost of Counseling: Rows l-o.</u>

The cost-effectiveness literature used assumptions for clinician time for counseling ranging from 5 to 15 minutes.[29;37;40;41;43] Two observations of clinician time for counseling have been reported. An average 90 seconds discussion time regarding tobacco was observed in usual practice in one study,[96] and average time of 31 minutes for smokers agreeing to participate in an RCT of NRT patches was reported in another.[55] The intensity of the latter study was beyond the scope for this report, so it was not used. Our estimate of the health benefits resulting from counseling was based upon estimates of the effectiveness of brief to medium intensity smoking cessation counseling. Most of the medium intensity interventions underlying our effectiveness estimates include longer periods of counseling delivered by staff that are less costly than physicians. Therefore, the cost of medium counseling was not necessarily substantially higher than brief counseling delivered by physicians if much of it is delivered by non-physicians. To approximate the costs of the mix of these interventions, we use an average of 2.5 minutes of physician time valued using 25% of the average of Medicare payment and median private sector charges for a 10 minute E&M visit,[97] adjusting to year 2000 dollars (row l). This average is intended to include the spectrum of smokers from those who receive very brief advice and are not receptive to assistance, to individuals who receive advice, assistance (including prescription), have follow-up arranged, and ask the provider multiple questions. In sensitivity analysis, the estimate of clinician time costs reflects a mean of 5 minutes of physician time and a range of 3 to 10 minutes.

Likewise we use an average of 25% of the value of patient time and travel for an office visit to approximate the average portion of such time that is attributable to tobacco cessation counseling across the mix of brief and medium intensity interventions. We assume that it takes 2 hours for travel and clinic appointment and we use average hourly earnings plus benefits in 2000[98] to estimate the value of patient time for a total of $22 per office visit (row m).

Smoking Cessation Aid Cost and Use: Rows p and q.

The cost of smoking cessation aids in typical practice is determined from data for HealthPartners members with a smoking cessation pharmacy benefit who filled a prescription for nicotine replacement therapy or bupropion (approved by HealthPartners Institutional Review Board). We estimate costs over a six-month period using 80% of the average whole sale price and a $7 dispense fee and found the average cost to be $170 (row p). The long term quit rate sub-model predicts that 16.3% of smokers who received advice in 2003 used a smoking cessation aid (row q). The most important data underlying this sub-model result are estimates of the use of smoking cessation aids among smokers who made a quit attempt in 1996[99] and 2001.[100] We use the estimate from the sub-model because we could not identify published data on the use of cessation aids among individuals who were advised to quit that could be generalized to all smokers in primary care settings.

Total Undiscounted, Costs of Cessation: Rows r-t.

We calculate the lifetime costs of counseling (row t) as the annual costs of counseling and smoking cessation aids, multiplied by the average number of years of life lived as a smoker (row s). The latter figure is calculated from the total number of years of life lived by active smokers in a birth cohort of 4,000,000, using BRFSS data by age group, divided by the estimated number of ever-smokers in a birth cohort of 4,000,000 tabulated for the CPB estimate as explained above.

E2. Cost-savings from Cessation:

The cost literature continues to debate whether or not smoking cessation reduces health care costs.[101-103] The debate centers on whether reductions in annual medical costs following cessation are offset by increased medical care costs due to increased life expectancy.[104;105] Very few CE studies of tobacco cessation interventions included savings from reduced medical expenditures.[106] Among those that provided an explanation for excluding these savings, most cite the conflicting evidence of lifetime savings.[37;38;41;43]

The fact that lifetime medical expenditures may increase due to increased life expectancy was not salient to our analysis. The methods established to maintain consistency across services in the prevention prioritization project[3;94] follow the convention of the larger body of preventive services CE studies in excluding unrelated medical costs from CE analyses. While the Panel on Cost-Effectiveness in Health and Medicine (PCEHM) was ambiguous about this point of methodology,[95] we adopted the convention for three reasons. First, most published CE studies exclude costs that are unrelated to the preventive service, so following this convention maintains comparability with the literature. Second, from the societal perspective, there is no reason to include medical expenditures associated with increased life expectancy but to exclude food, housing, transportation, or virtually any other resource use attributable to increased life expectancy. Third, including medical costs associated with increased life expectancy could produce counter-intuitive results such as high cost-effectiveness ratios for low cost, effective childhood vaccinations against common diseases with high case fatality rates.

Our method for estimating cost savings was to compare the annual health care expenditures of current and former smokers. Studies have reported that health care costs of former smokers can be higher than current smokers,[90;91;107] particularly shortly after cessation.[86;108;109] This is generally believed to be due to smokers who quit due to illness.[110;111] Studies have observed that resource use of former smokers falls below current smokers after 3 to 5 years.[86;108;109] One of these studies compared charges of former smokers 5 or more years after quitting with charges of current smokers.[86] The goal of repeated counseling is to induce and assist quits prior to the onset of SA illness. Therefore, the comparison of costs between current and former smokers for the purpose of estimating the CE of repeated counseling should exclude former smokers who quit due to onset of illness. For this reason, we base our estimates of the relative costs of current and former smokers on Musich et al., which is the only study identified in our literature search that reported total charges at various times since quitting, including quits 10 or more years prior to the observed expenditure period.

Annual Cost Savings for Former Smokers: Rows u-dd.

To determine SA costs in the U.S., we first parse per capita personal health care expenditures (PHE) into averages for never smokers, current smokers, and former smokers based upon algebraic manipulation of the relative costs calculated from Musich and the following equation: Average PHE in adults = % of never smokers × average PHE of never smokers + % current smokers × average PHE of current smokers + % of former smokers × average PHE of former smokers.

A recent study estimated average PHE by age group for 1999.[112] From these data, we calculate average PHE for persons 19 year of age or older and updated them to year 2000 (row u), using the percentage increase in total PHE for all persons from 1999 to 2000.[113] We utilize the smoking status from the BRFSS[62] for rows v-x. Using these data, we calculate average PHE per person according to smoking status, using the equations shown in source column for rows aa-cc, and we calculate the annual cost savings that would be achieved when a smoker becomes a former smoker as the difference between the PHE of current and former smokers (row dd).

Average Savings Per Quit: Rows ee-gg.

To obtain an estimate of lifetime savings of becoming a former smoker, we needed to know the average additional years of life for which an otherwise lifetime smoker would be a former smoker as the result of counseling. Data on the age distribution of quitting when counseled repeatedly over several years was not available. Therefore we use BRFSS data to estimate the average age of quitting in the current US population by comparing the age distribution of current and former smokers. We found that the average age of cessation is approximately 46. The life expectancy of the general population at this age is 33.5 years,[63] but the life expectancy of smokers is approximately 9 years fewer than non-smokers.[65] Therefore we approximate the years of life lived as a former smoker rather than as a continuing smoker following counseling to be 24.6 years (row ee) for each quit attributable to repeated counseling. This estimate may be conservative because repeated counseling may induce earlier quits than the spontaneous quits that make up a large portion of current quitters. Also, our overall calculation did not include additional years as a former smoker associated with quits that would eventually occur spontaneously in the absence of counseling, but would occur earlier with counseling.

We calculate undiscounted lifetime savings per additional quit (row ff) by multiplying the average annual savings by the average additional years spent as a former smoker. Then we calculate the average savings per ever-smoker counseled (row gg) by multiplying this estimate by the predicted lifetime effectiveness of repeated counseling from the long-term effectiveness sub-model (row j).

E3. Discounting and CE Calculation:

Because we were not building year-by-year Markov models, we employed alternate discounting techniques as described in our methods technical report.[3] To discount the costs of counseling and smoking cessation aid use, we estimate the median year of counseling after age 18 (row ff), based upon the age distribution of quitting among current smokers from the BRFSS.[62] Then we apply an appropriate discount factor based upon an annual discount rate of 3% (row ii) using present value tables developed for the Prevention Priorities Project.[3] Similarly, we apply discount factors corresponding to the years from age 18 at which additional years of life are realized and the years of prevented morbidity are realized (rows jj-mm). We estimate the years in the future at which additional years of life would be realized using average life expectancy[63] less 50% of the gains in life-expectancy tabulated for the CPB estimate (row b) and we assume quality of life gains from reduced morbidity would occur 5 years earlier (or about 2 years prior to the average smoking attributable death that is prevented).

Using these discount rates, we calculate lifetime costs of repeated counseling per ever-smoker, the medical care cost savings from quits, and the QALYs saved from quits discounted back to age 18 (rows pp-rr). The CE ratio (defined as net dollars per QALY saved) is not defined because *savings per QALY saved* is not a useful decision-making measure.[3] The net savings per ever-smoker is an estimated $542 in year 2000 dollars.

E4. Sensitivity Analysis for CE:

In single-variable sensitivity analysis, CE is highly sensitive to six variables:

- the effectiveness of repeated counseling in reducing tobacco use;
- the portion of 10-minute office visit costs attributable to counseling;
- the portion of those counseled who use a tobacco cessation aid;
- the ratio of PHE of never smokers over current smokers;
- the ratio of PHE of never smokers over former smokers; and
- the average years of smoking prevented per marginal quit.

Net costs per smoker counseled changes by at least 50% and as much as 425% in either the positive (lower net savings, positive net costs) or negative direction (higher net savings) with changes to each of these variables in the ranges for sensitivity analysis shown in Table 3. In the positive direction, changes to single variables produce CE ratios up to $14,300/QALY. The highest ratio is produced by assuming that the effectiveness of repeated counseling is equal to the 12-month effectiveness of a single counseling intervention. The largest change in the negative (-425%) occurs when tripling the effectiveness of repeated counseling.

Other variables to which CE is moderately sensitive (40% to 60% change in net costs with changes to variables inside their sensitivity analysis ranges) include:

- the costs of smoking cessation aids;
- the number of years of smoking in the birth cohort in the absence of counseling; and
- average PHE of all persons 19+ years of age.

In multivariate sensitivity analysis, the largest estimate in net savings from changing three variables simultaneously is $9,800 per smoker counseled from changing the effectiveness of repeated counseling, the ratio of PHE of never smokers over current smokers, and the ratio of PHE of never smokers over former smokers. Changing the same three variables in the opposite direction produces a cost-effectiveness ratio of $23,700/QALY. However, a slightly higher CE ratio of $28,100 is obtained by changing the effectiveness of repeated counseling, the portion of those counseled who use a cessation aid, and the ratio of PHE of never smokers compared to former smokers. Therefore, our overall range from multiple variable sensitivity analysis that we used as our key indicator of uncertainty of CE in comparing services is from $9,800 saved per person in the target population to $28,000/QALY.

F. Scoring

We ranked services in the Prevention Priorities project based upon scores for CPB and CE rather than point estimates.[3;114] For each measure, we assigned scores according to the quintile in which the service's CPB and CE estimates fell among all services included in the study scope. Services having the highest CPB or best-cost-effectiveness received a score of 5.

The base case estimate of 2,474,000 QALYs saved resulted in a CPB score of 5. The base-case was substantially higher than two other services receiving a score of 5 (at about 500,000 QALYs saved) and therefore large changes would be needed to reduce the CPB score to a 4. Our lower bound estimate from multivariate sensitivity analysis was 231,000, that would result in a CPB score of 4. This estimate was driven by reducing the estimate of effectiveness of repeated counseling in producing long-term quits from our base-case estimate of 23.1% to 2.8% (our estimate of the 12 month effectiveness of one-time counseling).

In the base-case, repeated counseling was cost savings. The model predicted that repeated counseling would generate net discounted costs of $542 per ever-smoker counseled. This estimate placed tobacco cessation counseling among five services that produced cost-savings and received a CE score of 5. Again, uncertainty in the effectiveness of repeated counseling creates moderate uncertainty in the CE estimate. Multivariate sensitivity analysis produced CE ratios as high as $28,000/QALY saved. At this level, the CE score would be 3.

The base case estimates produced a total score of 10, and the multivariate sensitivity analysis indicated a total score as low as 7 was possible, but only if the effectiveness of repeated counseling was substantially lower than the estimate used in our base-case estimates. If, for example, our base-case estimate for effectiveness was cut in half (to 11.5%), both the CPB and CE scores would remain at 5. In that scenario, the service would not be cost-saving, but it would be very cost-effective and tobacco cessation would remain in the top quintile of services for cost-effectiveness because no services with a CE score of 4 would be more cost-effective.

G. Limitations:

The model was very sensitivity to the effectiveness of counseling sub-model results. Due to instability of the sub-model to key data points, we used conservative estimates in the sub-model to calculate baseline effectiveness of repeated counseling. This does not, however, guarantee that the baseline estimate of effectiveness was conservative or that the resulting CPB and CE estimates were conservative. With these estimates, CPB and CE both received the highest scores of 5, yielding a total score of 10. Sensitivity analysis indicated that lower scores were feasible. We found that a total score of less than 9 was very unlikely unless the effectiveness of annual counseling was less than half of our base-case estimate.

The estimate of the relative savings achieved from smoking cessation was a secondary weakness because it was somewhat uncertain and moderately influential to the CE estimate. We based our estimate on the relative costs of former and current smokers from a single study. Sensitivity analysis indicated that annual counseling would be very cost-effective, but not cost-saving if we had based our estimates on the relative of costs from some of the other studies which we judged to have significant weaknesses relative to the included study. Although we found the relative costs from the included study to be consistent with estimates of the national health care expenditures that were attributable to smoking (as described above), more confidence in our CE estimates would be possible with additional high-quality studies that exam the relative costs of current and former smokers reported by time since last quit. Finally, because this was an influential variable, it was possible that a more detailed model based on specific costs by age and time since quit may produce somewhat different results.

We found no other limitations that were quantitatively important in sensitivity analysis. In the worst case scenario – with effectiveness of counseling equal to the 12 month quit rate of one-time counseling combined with the costs of annual counseling and low estimates of savings – brief tobacco cessation screening and intervention would receive a total score of 7 and still be considered by most to be a high priority service.

Table 1. Clinically Preventable Burden of Repeated Tobacco Cessation Counseling for Birth Cohort of 4,000,000 individuals				
		Base Case	**Data Source**	**Range for Sensitivity Analysis**
Gains in life expectancy				
a	Number of ever smokers in birth-cohort of 4,000,000	1,781,449	[62;63]	1,590,000 to 2,040,000
b	Average gains in LE per quit	5.65	[62;64;65]	+/-25%
Gains in Quality of life				
c	QALYs lost to smoking attributable (SA) illness in birth cohort	709,063	Table 2	+/-50%
d	QALYs lost to SA illnesses per ever-smoker	0.398	= c ÷ a	
e	Portion of ever-smokers who are former smokers	51.9%	[62]	+/- 5 % points
f	Relative risk of SA disease for former smokers compared to current ones	0.392	[65;86-88]	0.20 to 0.56
g	QALYs lost from SA morbidity per continuing smoker	0.581	= d ÷ (e×f + (1-e)	
h	QALYs saved from avoided morbidity per smoker counseled	0.353	= g - g×f	
Effectiveness and CPB				
i	Short-term (1 year) effectiveness of primary care interventions with/without medications	5.0/2.4%	[4-6;8-10;12;14;15;15-20;24-26]	2.0 to 8.0%/ 1.0 to 4.0%
j	Long-term effectiveness of repeated counseling in inducing additional quits among ever smokers	23.1%	sub-model	2.9% to 69.3%
k	CPB (total QALYs saved)	2,473,996	= a × (b+h) × j	

Table 2. QALYs lost to smoking attributable morbidity							
Condition	**Incidence Rate**	**SAF**	**SA Disease**	**Type of Incidence Data**	**Duration (yrs)**	**QALY Weight**	**SA QALYs Lost**
Cancers							
Oral Cavity, Pharynx	.000210	.646	22,325	New cases	4.3	0.2	19,200
Esophagus	.0000949	.681	10,644	New cases	1.8	0.3	5,748
Stomach	.000151	.207	5,152	New cases	3	0.2	3,091
Pancreas	.000216	.222	7,913	New cases	1.24	0.3	2,944
Larynx	.0000727	.805	9,637	New cases	2	0.3	5,782
Lung, Bronchus	.00124	.803	163,299	New cases	2	0.3	97,979
Urinary Bladder	.000424	.404	28,193	New cases	4.7	0.2	26,501
Kidney, Renal Pelvis	.000242	.259	10,311	New cases	4.7	0.2	9,692
Acute Myeloid Leukemia	.0000788	.170	2,204	New cases	4.6	0.2	2,028
Cervix Uteri	.000151	.120	1,555	New cases	4	0.2	1,244
Circulatory Diseases							
Ischemic Heart Disease	.0147	.164	396,975	Hospital stays	.058	0.3	6,871
Other Heart Disease	.00797	.125	164,364	Hospital stays	.058	0.3	2,845
Congestive Heart Failure	.00387	.125	79,859	New cases	2.3	0.2	36,735
Strokes	.00352	.102	58,783	1st strokes	7.8	0.4	183,403
Transient Ischemic Attack	.00147	.102	24,571	Hospital stays	.058	0.3	425
Atherosclerosis	.000774	.143	18,256	Hospital stays	.058	0.3	316
Aortic Aneurysm	.000443	.575	41,926	Hospital stays	.058	0.3	726
Other Arterial Disease	.000711	.134	15,620	Hospital stays	.058	0.3	270
Respiratory Diseases							
Pneumonia, Influenza	.0429	.169	1,192,136	Self-reported	.038	0.3	13,755
Bronchitis, Emphysema, Chronic Airways Obstruction	.00169	.785	218,910	New cases	6.6	0.2	288,961
Injuries							
Fire Injuries	.0000485	.25	3,596	Injuries	.077	0.3	83
Childhood Diseases							
Short Gestation/Low Birth Weight	.0150	.0907	5,434	Hospital stays	0.25	0.3	408
Respiratory Distress Syndrome	.00815	.0346	1,128	Hospital stays	.167	0.3	57
Other Respiratory – newborn	.0244	.0472	4,618	Hospital stays	.167	0.3	231
TOTAL							**709,063**

Table 3. Cost Effectiveness of Repeated Tobacco Cessation Counseling				
		Base Case	**Source**	**Range for Sensitivity Analysis**
Cost of counseling				
l	Cost of 10-minute office visit	$ 44	[97]	+/- 33%
m	Cost of patient time and travel for office visit	$ 42	[98]	+/- 50%
n	Portion of office visit needed for counseling	25%	assumed	10% to 50%
o	Total cost of counseling per occasion	$22	= (l + m) * n	
p	Average cost of smoking cessation aids per quit attempt	$170	study data	+/- 50%
q	Portion of counseled who use a smoking cessation aid	16.3%	sub-model	10% to 30%
r	Number of years as smokers in birth-cohort of 4,000,000	47,261,827	[62]	+/- 20%
s	Average years as smoker, per ever-smoker	26.5	= r ÷ a	
t	Lifetime costs of counseling and smoking cessation aid use per ever-smoker counseled, undiscounted	$ 1,308	= (o + q×p) × s	
Cost-savings				
u	Per capita personal health care expenditures (PHE) if 19+ in 2000	$ 6,957	[112;113]	0.40 to 0.55
v	Ever-smokers as % of population	0.466	[62]	0.20 to 0.27
w	Current smokers as % of population	0.224	[62]	+/- 20%
x	Former smokers as % of population	0.242	= v - w	
y	Ratio of average PHE for never compared to current smokers	0.76	[86]	0.65 to 0.85
z	Ratio of average PHE, for never compared to former smokers	0.86	[86]	0.75 to 0.95
aa	Average annual PHE of current smokers	$ 8,291	= u ÷ ((1-v) × y + x×z + w)	
bb	Average annual PHE of never smokers	$ 6,329	= y × aa	
cc	Average annual PHE of former smokers	$ 7,379	= bb ÷ z	
dd	Annual cost savings per additional year as former smoker	$ 912	= aa - cc	
ee	Number of current smoker years converted to former smoker years by counseling per smoker	24.6	[63 65]	+/- 25%
ff	Average lifetime savings per additional former smoker	$ 22,434	= dd × ee	
gg	Average savings per ever-smoker counseled	$ 5,188	= ff × j	
Discounting and CE calculation				
hh	Median year of counseling after age 18	26	[62]	
ii	Corresponding discount factor	0.464	[3]	+/- 20%
jj	Median year of life year saved after age 18	56.1	[63-65]	
kk	Corresponding discount factor	0.191	[3]	+/- 20%
ll	Median year of morbidity & cost prevention after age 18	51.1	= jj - 5	
mm	Corresponding discount factor	0.221	[3]	+/- 20%
nn	Discounted lifetime counseling and smoking cessation aid costs per ever-smoker counseled	$ 607	= t × ii	
oo	Discounted lifetime savings per ever-smoker	$ 1,149	= gg × mm	

	counseled			
pp	Discounted QALYs saved per ever-smoker counseled	0.268	= (h×mm + b×kk) × j	
qq	CE	not defined	= (nn - oo) ÷ pp	
rr	Discounted net cost per ever-smoker	$ -542	= nn - oo	

APPENDIX : Long-Term Quit Rate Sub-Model

We developed a sub-model to our CPB model estimate which answers the question "What long-term quit rate for repeated counseling is consistent with:

a) trends in counseling delivery rates
b) trends in total quits among smokers
c) trends in spontaneous quits, and
d) the 12-month counseling effectiveness of brief to medium counseling obtained from the literature review described above?

Equations 1) and 2) show how the sub-model determines the long-term effect of repeated counseling:

1) $$\text{LTMQRC} = \sum_{t=1}^{\infty} MQRC_t = MQRC_{t-1} \times e^{-\alpha t}$$

2) $$\text{LTMQRC}_{\text{RX}} = \sum_{t=1}^{\infty} MQRCRX_t = MQRCRX_{t-1} \times e^{-\alpha t}$$

These equations defined the long-term effectiveness of repeated counseling as an exponential function of the 1-year quit rates. *LTMQRC* and $LTMQRC_{RX}$ were the marginal long-term quit rates of brief to medium counseling with and without smoking cessation aids (respectively), and $MQRC_t$ and $MQRCRX_t$ were the marginal quit rates of brief to medium counseling with and without smoking cessation aids in year t^{th} following counseling. For these variables, the margin was defined as the quit rate in a population receiving repeated interventions group minus the expected quit rate from self-initiated quit attempts. Self-initiated quit attempts were all quit attempts, with or without the use of smoking cessation aids that were initiated by the smoker prior to discussion with a clinician.

In Year 1, $MQRC_t$ and $MQRCRX_t$ were equal to the 12-month marginal quit rates found in our evidence review (2.4% and 5.0%). The constant *e* was 2.71828 (the base of the natural logarithm) and alpha was an unobserved constant that was determined by the other data points in the sub-model. The exponential function was equivalent to the inverse of the natural logarithm. It was used in modeling applications to describe processes that begin as a positive number and decline over time without falling below zero, although the function may increase over time (away from zero) if alpha was negative or remain constant over time if alpha was zero.

The long-term quit rate sub-model was summarized in equation 3). It defines the cumulative quits in a cohort of smokers starting in year *t* and ending in year *u*.

3) $$LTQR = \sum_{t=1}^{u} PS_{t-1} \times (SQR_t + C_t \times MQRC_t + CRX_t \times MQRCRX_t)$$

LTQR was the observed long term total quit rate of a cohort of smokers, including quits attributable to clinician counseling and quits not attributable to clinician counseling ('spontaneous quits'). PS_{t-1} was the portion of the cohort still smoking at the end of the previous year; SQR_t was the self-initiated quit rate in year *t* less relapse over subsequent years (the 'permanent' self-initiated quit rate). C_t was the portion of smokers who receive counseling in year t and do not use a pharmacologic smoking aid; and CRX_t was the portion of smokers receiving counseling and who do use a quit aid.

With algebraic substitutions from equations 1) and 2), equation 3) became:

$$4)\ LTQR = \sum_{t=1}^{u} PS_{t-1} \times (SQR_t + C_t \times MQRC_{t-1} \times e^{-\alpha t} + CRX_t \times MQRCRX_{t-1} \times e^{-\alpha t}).$$

In year zero, *PS* was equal to 1 (eg 100% of smokers are still smoking at end of the year), and in subsequent years *PS* was determined within the model by the number of self-initiated quits and counseling-attributable quits in prior years, less relapse among counseling-attributable quits from prior years. All variables other than *PS* and alpha can be estimated from available data as described below. Therefore, we solved for α in equation 4) by iteration and then inserted α into equations 1) and 2) to estimate the long-term quit rates with repeated counseling. We did not separately model new quits and relapse among those previously counseled. Instead we allowed the constant α to reflect the quits in subsequent periods, net of relapse of individuals who had previously quit for one year as a result of counseling.

We modeled a cohort of smokers over 39 years (u = 39) from 1965 through 2003. However, as described below, we determined alpha using observed long-term quits over the period 1985 to 2003. This allowed us to estimate the model over the period for which better data were available and at the same time account for the effect of counseling that began prior to 1985.

Data points of sub-model

For data points in the Prevention Priorities project, we used estimates for the base case that, as accurately as possible, reflected true U.S. experience. However, in a sensitivity analysis of the sub-model, we observed a tendency for the model to predict very high long-term effectiveness (up to 100%) from small changes in some key underlying data points. In order to guard against such a large overstatement of the long-term effectiveness of repeated counseling, some of the data points used in our base case were conservative.

Spontaneous quit rates

Self-initiated quits have not been directly observed over multiple years, so it was not possible to make direct observations of long-term relapse rates. Therefore, to estimate permanent spontaneous quits, we estimated annual spontaneous quit attempts and then estimated what portion of these would result in long-term cessation from available survey data.

Although self-initiated quit attempts may have trended upward since 1965, there was little data available to support this belief. The BRFSS and NHIS only began asking questions about quit attempts in the early 1990s, and there was no apparent upward trend in the responses to these questions since then. Discerning any trend was made more difficult by the fact that early surveys asked only if smokers quit for at least a day, and later surveys asked if smokers quit for at least a day in an effort to quit smoking. Therefore, in our base-case we calculated the average quit attempts from published summaries over the 1990s[115-118] and applied that estimate (45.2%) to all years in the sub-model.

The estimate of 43.5% of smokers making a quit-attempt reflects both self-initiated quit attempts and quit attempts attributable to counseling. To estimate the portion of these quit attempts that were spontaneous quit attempts, we obtained an estimate of the relative risk of quit-attempts of those counseled compared to those not counseled from estimates reported from the 1990 California Tobacco Survey.[119] Smokers who reported having been advised to quit by a physician were approximately 16% more likely to make a quit attempt (RR = 1.16). We estimated the portion of quit attempts that could be attributable to counseling using this relative risk and the estimates of counseling delivery rates (below).

Finally, to determine the number of permanent self-initiated quits, we multiplied each year's self-initiated quit attempts by an estimated long-term success rate, which we derived from the literature. Our base-case estimate of the long-term success rate was derived by multiplying an estimate of 12-month success rates from a published summary estimate of 6 prospective studies in which smokers whose only study-related contacts regarding cessation were survey questions regarding smoking behavior.[120] The review found an average 4.3% success rate for spontaneous quits at 12-months.

This estimate reflected the success rate prior to the introduction of effective smoking cessation aids (NRT and bupropion). Smokers who self-initiate quit attempts may seek prescriptions for cessation aids or may purchase over-the-counter NRT products. For the self-initiators who use a tobacco cessation medication, we added the difference between our 12-month marginal quit rates of counseling with cessation medication use and counseling alone (5.0% - 2.4% = 2.6%) to derive a 12-month success rate of 6.9%.

For both self-initiators who use a cessation product and those who do not, we assumed a 37% long-term relapse rate among those who remained non-smokers at 12 months. This estimate was reported in the 1990 Surgeon General's Report on the Health Benefits of Smoking Cessation,[121] based on data from the National Health and Nutrition Examination Survey, Epidemiologic Follow-up Survey. Therefore, in our base case we used a long-term success rate for self-initiated quits without the use of smoking cessation aid of 4.3% x (100%-37%) = 2.7%, and a long-term success rate of 6.9% x (100%-37%) = 4.2% with the use of smoking cessation aids.

Frequency of clinician counseling

Counseling rates increased over the years for which data were available. We fit a linear trend to the available data between 1991 and 2002. We then extended the trend backward through time using the negative of annual percentage change in per capita cigarette consumption[122] as a proxy for the percentage change in counseling rates prior to 1991.

The long-term quit rate sub-model also required an estimate of that portion of clinician counseling that resulted in the smoker making a quit attempt with the use of a smoking cessation aid. We identified two estimates of the use of smoking cessation aids among all smokers: NRT use in 1996[99] and NRT and bupropion use in 2001.[100] We excluded one similar estimate[123] because it reported the average for quit attempts over several years, and NRT was available for only a small number of these years. We first fit a linear trend from zero in 1985 (prior to the introduction of nicotine gum) through these two data points. The resulting trend reflected all use, not just use prompted by clinician advice. To derive an estimate of cessation aid use resulting from clinician advice alone, we used the relative risk of making a quit attempt following counseling from Gilpin et al (1.16)[119] as a proxy for the relative risk of using a smoking cessation aid. As with total quits, we used this relative risk to parse each year's estimate of the use of smoking cessation aids into use prompted by clinician advice and use for self-initiated quits. The result was a linear increase over time that reaches 16% in 2003 in the portion of all those counseled who use a cessation aid.

Long term quit rates

In the long-term effectiveness sub-model, counseling cannot produce more quits than the difference between total quits and spontaneous quits. Therefore, the total long-term quit rate provided an important upper bound on the estimate of the long-term effectiveness of repeated counseling. In the literature, long-term quit rates are often calculated as the portion of ever-smokers who are now former smokers. This calculation has been called the quit ratio[121] or cessation prevalence.[124] The measure was imperfect for older age groups, because tobacco related deaths disproportionately exclude continuing smokers from the denominator. It was also poorly suited for our purposes because the peak prevalence in smoking for some age groups occurred before the first year in the sub-model. For these reasons, we used a related but more reliable measure of long term quit rates to estimate alpha in equation 3. We compared current smoking rates of the BRFSS sample representing persons 18-54 years of age in 1984 with current smoking rates of their corresponding age groups 20 years later in the 2003 BRFSS (ages 34-74). We down-weighted individuals in the older age group (aged 65-74 in 2003) and excluded the oldest age group (age 75+) to reduce the impact of survival bias. The comparison of these samples indicated that approximately 31% of current smokers aged 18-54 in 1984 quit by 2003. We adjusted this estimate down to reflect an estimated 10% of former smokers who stop smoking cigarettes but use other tobacco products,[121] giving a final estimate of 28%.

Without an adjustment for survival bias, older age groups appear to have higher quit rates. Therefore, depending on the extent of survival bias, reducing the influence of older age groups in our calculation may have produced a low estimate of total quits between 1984 and 2003. If this was the case, it would cause our sub-model to produce a conservative estimate of the long-term effectiveness of repeated counseling, and that seems desirable.

Calculation of alpha and results

We used iteration to solve equation 3) for an α that was consistent with this 28% decline in smoking among the model cohort between 1984 and 2003 (ie. $(PS_{2003} - PS_{1984})/PS_{1984}$ = -28%). In addition to providing the best possible estimate total quits, the period 1984-2003 included more accurate estimates of delivery rates and included the period in which NRT and bupropion were introduced as smoking cessation aids.

Sub-model results

The sub-model produced $\alpha = 0.125$, which yielded estimates for the long-term effectiveness of repeated counseling of 20.2% without the use of cessation aids, and 38.0% with the use of cessation aids. With 16.3% of those counseled choosing to use a cessation aid in the final year of the model, the weighted estimate of the effectiveness of long-term repeated counseling was 23.1%.

Sensitivity analysis for sub-model

We explored the sensitivity of the sub-model's estimate of the long term effectiveness of repeated tobacco cessation counseling to the sub-model's main variables: 12-month quit rates with and without the use of smoking cessation aids, counseling rates, the rate of annual quit attempts, the rate of success of self-initiated quit attempts, and total long term quits. Detailed reporting of the results of the sensitivity analysis were warranted due to the instability revealed.

We changed the 12-month marginal quit rates for counseling with and without the use of a smoking cessation aid in a quit attempt. We varied both marginal quit rates together in sensitivity analysis under the assumption that if our literature review resulted in an overstatement or understatement of one marginal quit rate, it also over- or understated the other. We varied the 12-month marginal quit rate for counseling in which no cessation aid was used from 1.0% to 4.0% (base case 2.4%) and the marginal quit rate for counseling in which a cessation aid was used from 2.0% to 8.0% (base case 5%). Thus, we re-estimated the sub-model using 1.0% and 2.0% at the low end of these ranges, 4.0% and 8.0% at the high end, and several combinations in between. The resulting range of long-term quit rates was 19.9% to 26.3% (base case result: 23.1%).

We explored the sensitivity of the long-term quit rate to trends in counseling rates by changing the rate for 2003 in the sub-model and then estimating the trend in prior years as in the base-case. We solved the sub-model with 2003 counseling rates from 30% to 65% (base case 52%) and obtained a corresponding range of long-term quit rates of 18.6% to 47.6%. Higher counseling rates in the sub-model produce lower predicted long-term counseling effectiveness estimates because a higher success rate was required to explain the difference between total quits and self-initiated quits. We viewed the counseling rates used in the base case as being conservative because they were likely to include a larger amount of smoker-reported counseling that falls short of the intent of the five A's (ask, advise, assess, assist, and arrange) as recommended by the USPSTF.[125] In addition, when asked within a week of an office visit, smokers tended to overstate receipt of advice by 20% to 50%.[126;127] Therefore, we performed an additional sensitivity analysis in which we compared the counseling rate trend we computed to the results of three studies that measured the frequency of counseling when it was delivered in a manner more consistent with completing the five A's to an appropriate point for each smoker. These studies used either direct observation of office visits[96;128] or physician-completed encounter forms.[129] The counseling rates computed by these studies were approximately 50% lower than our trend line in the same years (1991 to 1998). In sensitivity analysis, we reduced our trend in counseling delivery rates by this amount and extended the trend to previous decades with the same adjustments we made to trends in spontaneous quit rates. At the same time, we made a corresponding adjustment to the relative risk of making a quit attempt with counseling to reflect lower levels of five A counseling in the sample on which the relative risk was observed.[119] With these lower counseling rates the sub-model was unable to find a solution of long-term effectiveness below 100%.

Total quit attempts in the sub-model were an important determinant of the number of self-initiated quit attempts and ultimately the number of successful self-initiated quits. In the base-case, we applied a constant quit attempt rate of 42.5%. In sensitivity analysis, we first varied this constant rate from 30% to 55%. At 30% annual quit attempt rate, the long-term effectiveness estimate jumped to 74% and at a 55% annual quit attempt rate the model was unable to find a solution because the long-term quit rate would need to be negative for an annual quit rate of 55% to be feasible. We viewed the base-case quit attempt rate as a conservative estimate. Lower quit attempts in earlier years (when counseling rates were lower) produced higher long-term quit rates in the sub-model. Because quit attempts may have increased over time to present rates as the dangers of smoking have become widely known and cigarette prices have increased, we performed a second sensitivity analysis by estimating a trend of quit attempts that starts low in 1965 and increases over time to the rates of the late 1990s. The trend was estimated to correspond to declining per capita cigarette consumption in the US over this time period.[122] The resulting long-term effectiveness estimate was 54.9%.

The second important determinant of self-initiated quits was the long-term success rate of those who attempt a self-initiated quit. In the base-case, we employed separate estimates for success rates of self-initiated quits with and without the use of a cessation aid (5.8% and 2.7% respectively). We varied these rates simultaneously in sensitivity analysis in the same way we varied the 12-month quit rates of counseling with and without the use of cessation aids. There were no solutions below 100% effectiveness for self-initiated quit success rates at or below the combination of 3.0% and 1.0% (with and without cessation aids), and no solution above zero percent at or above the combination of 7.0% and 3.5%.

The base case estimate of 2.4% long-term success of spontaneous quits without the use of a cessation aid was based upon an estimate of 12-month success of 4.3%. As part of our sensitivity analysis we used an update of the 4.3% estimate for the success rate without use of a smoking cessation aid.[130] Among the new studies included in the update, only one reported quit rates at 12 months. The authors of the update were not definitive about whether their updated results were representative of 6 month or 12 month quit rates. For sensitivity analysis, we interpreted their result of 3-5% to be a 6 month success rate and used the midpoint of 4% in our calculations. We then applied an estimate of 25% relapse between 6 and 12 months, which was calculated as the average of six studies in the review by Cohen et al. and five more recent studies.[99;131-134] Finally, we applied the same 37% relapse rate after 12 months and obtained an estimate for sensitivity analysis of 1.9% long-term success rate among self-initiators who do not use a cessation product: 4% x (1-25%) x (1-37%) = 1.9%. The corresponding quit rate for success with a cessation product, calculated in the same way as for the base case, was 3.4%. This combination yielded an estimated long-term effectiveness estimate of 71.3%

Finally, we explored the sensitivity of the sub-model results to changes in the number of total quits between 1984 and 2003 by solving the model for a wide range of total quits in place of our base-case quit rate of 28%. The sub-model was unable to identify a long term counseling effectiveness above zero percent for 1984-2003 quit rates of 24% and below and was unable to find long term effectiveness rates below 100% for 1984-2003 total quit rates above 39%.

It was clear from the single-variable sensitivity analysis that the long-term effectiveness estimates were extremely sensitive to the estimates of total quit attempts, the success rate of self-initiated quits and the number of long-term quit attempts among current smokers in 1984 by 2003. Table A1 demonstrates the instability of the sub-model to changes in two of these variables, total quit attempts and total successful quits between 1984 and 2003. The table shows the results of the single-variable sensitivity analysis described above for these variables, as well as the results of changing both variables at the same time. For example, changing the estimate of annual attempts to 37.5% produced a long term effectiveness estimate of 49.5%; changing the estimate of total quits between 1985 and 2003 to 31% produced a long-term effectiveness estimate of 46%; and making both of these changes produced a long-term effectiveness estimate of 71.4%.

Table A1. Two-variable Sensitivity Analysis of Long-term Effectiveness

Annual Attempts	Long-term effectiveness	Total Quits 1984 to 2003	Long-term Effectiveness	Long-term Effectiveness with Change in Both Quit Attempts and Total Quits
30.0%	74.4%	34%	69.2%	no solution
32.5%	66.2%	33%	61.7%	100.0%

35.0%	57.6%	32%	54.4%	86.9%
37.5%	49.5%	31%	46.1%	71.4%
42.0%	40.6%	30%	38.4%	49.1%
42.5%	32.4%	29%	30.9%	40.0%
45.2%	**23.1%**	**28%**	**23.1%**	**23.1%**
47.5%	15.3%	27%	16.2%	8.8%
50.0%	8.2%	26%	9.4%	no solution
52.5%	3.0%	25%	4.4%	no solution

Limitations of the sub-model:

A wide range of long-term effectiveness estimates can be generated by making small changes to combinations of total quit attempts, the success of spontaneous quit attempts, and the total quit rate for which the sub-model was solved. The long-term effectiveness estimate was also moderately sensitive to changes in the delivery rates of counseling over the time period in the model. In particular, these changes to these variables could lead to explosively high estimates of long-term effectiveness. We used conservative estimates to guard against this possibility, but given the high instability of the model, it was not necessarily the case that the resulting estimate of long-term effectiveness of repeated counseling was also conservative. In general, the sub-model failed to provide much insight into the estimate of long-term effectiveness other than indicating that a broad range of estimates were consistent with recent trends.

Some choices made in the model structure were relatively unimportant while the importance of other model characteristics was unknown. Because the functional form describes the average experience among a cohort of smokers, it seemed reasonable to suppose that the largest impact was in the fist year of counseling and the impact declines thereafter, even though some smokers within the cohort would be more receptive to advice in later years. This pattern was observed in the two studies of repeated intensive interventions noted in introduction of this appendix.[92;93]

We made three other potentially important simplifications that were necessary to create a model for which a mathematical solution exists. First, we restricted α to be equal in equations (1) and (2) because we lacked data on the relative differences in impact of counseling with and without smoking cessation aids after the first 12 months. Second, rather than modeling relapse separately, we allowed α to reflect net quits in subsequent years. Finally, as counseling rates increased over time, the model implicitly assumed that individuals who were counseled in the previous year were also counseled in subsequent years unless they quit smoking. Therefore, each year's increment in advice to quit smoking was assumed to be provided either to smokers who were not previously counseled or smokers who were counseled, quit, and then relapsed. In reality, some smokers will not receive counseling every year until they quit, particularly those who go through a year without making a visit to a health care provider.

Other discussion for sub-model:

For each of the four variables to which the sub-model was moderately to highly sensitive, we believe that our base case estimates were more likely to be conservative than not. In estimating the total quit rate by 2003 of smokers in 1984, we substantially down-weighted the older age groups. We assumed that total quit attempts were at the self-reported rates of the 1990s even though it was plausible that quit attempts were less common in early decades. We used the available literature to calculate two different sets of success rates for self-initiated quit attempts and used the more conservative estimate in our base case. Similarly, we used the more conservative trend in delivery rates rather than the trend adjusted to reflect counseling consistent with five A's of counseling.

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