# Chapter 5
# The Benefits of Smoking Cessation on Overall Morbidity, Mortality, and Economic Costs


**Introduction** *439*

**Benefits of Smoking Cessation on Overall Morbidity** *439*

Conclusions from Previous Surgeon General's Reports *439*
Description of the Literature Review *440*
  Assessment of Morbidity *440*
  Assessment of Smoking Status *440*
Epidemiologic Evidence *457*
  Cross-Sectional Studies *457*
  Longitudinal Studies *458*
Synthesis of the Evidence *460*
Summary of the Evidence *460*

**Benefits of Smoking Cessation on All-Cause Mortality** *461*

Conclusions from Previous Surgeon General's Reports *461*
Summary of the Evidence *464*

**Benefits of Smoking Cessation on Economic Costs** *465*

Economic Costs of Smoking *465*
Economics of Smoking Cessation *466*
  Principles of Cost-Benefit and Cost-Effectiveness Analysis *467*
  Cost-Effectiveness of Clinical Smoking Cessation Interventions *467*
  Cost-Effectiveness of Nonclinical Smoking Cessation Interventions *482*
  Cost-Effectiveness of Tobacco Price Increases Through Taxation *482*
Synthesis of the Evidence *482*

**Summary of the Evidence** *485*

**Conclusions** *485*

**References** *486*

# Introduction

Cigarette smoking causes multiple diseases and reduces the general level of health of smokers (U.S. Department of Health and Human Services [USDHHS] 2004, 2014). These health consequences have been well documented in previous Surgeon General's reports. The 1964 report first summarized results on smoking and all-cause mortality, finding that smoking causes a 70% increase in risk of adverse health consequences (U.S. Department of Health, Education, and Welfare [USDHEW] 1964). The 2004 report found smoking generally diminishes health (USDHHS 2004). General measures of health can be informative because they provide an integrative indicator of the health burden placed on smokers and on society overall. In addition to the direct human costs that smoking places on persons and society, one general measure with acknowledged implications for public health policy and practice is the economic cost of smoking.

This chapter considers broad indicators of burden in relation to smoking cessation, including morbidity, mortality, and economic costs. Initially, it considers how general indicators of health can change after smoking cessation. This type of information is critical to informing smokers about the potential benefits of cessation and serves as a strong rationale to provide interventions that can help increase the success of quitting smoking. Such programs may be offered through healthcare organizations, communities, states, and other organizations. Smoking is known to generate healthcare and other economic costs and to affect the economics of the households of smokers (USDHHS 2014). Previous Surgeon General's reports on tobacco have periodically reviewed the economic costs of smoking, as tracked by the Centers for Disease Control and Prevention's (CDC's) Smoking-Attributable Mortality, Morbidity, and Economic Costs (SAMMEC) model. This chapter expands on this work by focusing on the most recently available scientific literature on the economic benefits of smoking cessation, while also complementing the kinds of cost estimates previously provided by SAMMEC.

# Benefits of Smoking Cessation on Overall Morbidity

Chapter 4 of this report (The Health Benefits of Smoking Cessation) describes the associations between smoking cessation and changes in risk for specific disease outcomes. It also addresses how cessation affects the natural history of various disease outcomes, such as by slowing the progression of underlying pathophysiological processes. In addition to the beneficial impacts on specific disease outcomes, previous reviews of smoking cessation and morbidity (Goldenberg et al. 2014) have concluded that cessation is associated with improvement in health-related quality of life (HRQoL), a broad construct defined by *Healthy People 2020* as "a multi-dimensional concept that includes domains related to physical, mental, emotional, and social functioning" (Office of Disease Prevention and Health Promotion 2018). In a complementary conclusion, after evaluating a broad range of general evidence, the 2004 Surgeon General's report concluded that active smoking is causally associated with diminished health status (USDHHS 2004).

This chapter addresses the evidence on smoking cessation and its relationship to more general measures of health outcomes, particularly whether cessation improves general QoL compared with continued smoking. This review aligns with and complements the approach used in previous Surgeon General's reports on smoking, including the 2014 Surgeon General's report (USDHHS 2014). However, to limit the scope of this review, some of the many correlates of well-being (e.g., absenteeism from work) are not specifically considered.

## Conclusions from Previous Surgeon General's Reports

Previous Surgeon General's reports (USDHHS 1990, 2004) have comprehensively covered the relationship between smoking and general morbidity. The 1990 Surgeon General's report on the health benefits of smoking cessation synthesized scientific evidence about cessation and its effects on general morbidity, concluding that "former smokers have better health status than current smokers as measured in a variety of ways, including days of illness, number of health complaints, and self-reported health status" (USDHHS 1990, p. 9). However, that report also found that the reviewed studies were "extremely heterogeneous, with some methodologic shortcomings" (USDHHS 1990, p. 89) and that the "variety of measures used makes direct comparison across studies problematic" (USDHHS

1990, p. 87). The 2004 Surgeon General's report on the health consequences of active smoking subsequently reviewed studies that included various indicators of general health, concluding that "the evidence is sufficient to infer a causal relationship between smoking and diminished health status that may be manifest as increased absenteeism from work and increased use of medical care services" (USDHHS 2004, p. 676). In addition, a major conclusion of the 2004 report was that "quitting smoking has immediate as well as long-term benefits, reducing risks for diseases caused by smoking and improving health in general" (USDHHS 2004, p. 25). The present chapter updates these findings on the basis of more recent studies of smoking cessation and indicators of general morbidity.

## Description of the Literature Review

Scientific literature from 1990 to 2017 was systematically reviewed, and reference lists from the identified articles were searched for additional studies. Search terms included "smoking cessation," "epidemiology," "morbidity," "health status," and "quality of life." Studies were included if they measured the benefit of smoking cessation for general morbidity in former cigarette smokers; thus, the appropriate comparison group was continuing cigarette smokers but not never smokers. Accordingly, only studies that specifically and directly compared outcomes between former cigarette smokers (defined in multiple ways) and current cigarette smokers were considered. Studies that included former cigarette smokers but used only never smokers as the reference group were not included because such studies were not informative for the purpose of this chapter. However, when informative comparisons were made in eligible studies that met the criterion of comparisons with current smokers, some findings for never smokers were included.

Following the systematic review of literature, 24 studies published from 1995 to 2016 were identified that assessed smoking cessation and general morbidity, including 7 cross-sectional studies (Table 5.1) (Tillmann and Silcock 1997; Olufade et al. 1999; Mulder et al. 2001; Bolliger et al. 2002; Mody and Smith 2006; Heikkinen et al. 2008; McClave et al. 2009) and 16 prospective cohort studies (Tables 5.2–5.4) (Stewart et al. 1995; Taira et al. 2000; Bolliger et al. 2002; Zillich et al. 2002; Erickson et al. 2004; Mitra et al. 2004; Croghan et al. 2005; Wiggers et al. 2006; Jensen et al. 2007; Rungruanghiranya et al. 2008; Gutiérrez-Bedmar et al. 2009; Balduyck et al. 2011; Papadopoulos et al. 2011; Hays et al. 2012; Piper et al. 2012; Tian et al. 2016).

### Assessment of Morbidity

The general measures of morbidity used in the 24 identified studies varied but cover three main categories: general, smoking specific, or disease specific:

1. **General.** Many studies used general measures of HRQoL, most frequently the Short Form (SF)-36 (SF-36) and SF-12 surveys, both the Medical Outcomes Study (Ware Jr and Sherbourne 1992) and RAND versions (Hays and Morales 2001). One study (Mitra et al. 2004) adapted the SF-36 for use in a population with mobility impairments. The other generic measures of HRQoL included the 15-D (dimensional) (Sintonen 1995), the EuroQoL (The EuroQol Group 1990), the QoL Inventory (Frisch et al. 1992), the World Health Organization's QOL-BREF (Skevington et al. 2004), CDC's HRQOL-4 and its Healthy Days Symptoms Module (Moriarty et al. 2003), and the Functional Status Questionnaire (Jette et al. 1986). The studies identified in the literature review also assessed dissatisfaction with life and general health status.

2. **Smoking specific.** One study (Olufade et al. 1999) used the Smoking Cessation Quality of Life (SCQoL) questionnaire.

3. **Disease specific.** Some studies used disease-specific measures of HRQoL. These measures assess the impact of specific diseases on relevant components of QoL. The European Organisation for Research and Treatment of Cancer (EORTC) QoL Questionnaire QLQ-C30 (Aaronson et al. 1993) was used, along with the LC13 module for lung cancer (Bergman et al. 1994) and the H&N35 module for head and neck cancer (Bjordal et al. 1994). Other disease-specific instruments included the Aquarel questionnaire for patients with pacemakers (Stofmeel et al. 2001), the Clinical COPD Questionnaire (van der Molen et al. 2003), and the VascuQoL questionnaire for patients with peripheral arterial disease (Morgan et al. 2001).

### Assessment of Smoking Status

Most of the 24 identified studies assessed cigarette smoking status by self-report. Self-reported smoking status continues to be sufficiently valid and reliable for studying the general population but may be less accurate for assessing smoking in high-risk or medical patients (Velicer et al. 1992; USDHHS 2004, 2014).

**Table 5.1 Cross-sectional studies about smoking status and quality of life**

| Study | Design/population | Smoking status | Health status measure | Outcomes/findings | Comments |
|---|---|---|---|---|---|
| Tillmann and Silcock (1997) | • Cross-sectional study<br>• Current smokers and ex-smokers randomly selected from records of nine general practices<br>• n = 3,000<br>• 1995<br>• Scotland | • Current smokers (n = 1,500)<br>• Ex-smokers of 5 years or more (n = 1,500) | • SF-36<br>• EuroQoL tariff scores | • HRQoL, as measured by SF-36 and EuroQoL tariff scores, was significantly higher for ex-smokers than for current smokers.<br>• Mean difference by measure and QoL dimension:<br>– EuroQoL tariff: 0.03 (95% CI, 0.011–0.058), p = 0.004<br>– Physical functioning: 3.93 (95% CI, 1.267–6.585), p = 0.004<br>– Role-physical: 4.52 (95% CI, 0.519–8.516), p = 0.027<br>– Bodily pain: 3.10 (95% CI, 0.508–5.698), p = 0.019<br>– General health: 5.32 (95% CI, 3.027–7.611), p = 0.000<br>– Vitality: 5.41 (95% CI, 3.348–7.469), p = 0.000<br>– Social functioning: 4.36 (95% CI, 1.015–6.810), p = 0.000<br>– Role-emotional: 4.77 (95% CI, 0.960–8.588), p = 0.014<br>– Mental health: 5.13 (95% CI, 3.401–6.907), p = 0.000 | — |

**Table 5.1 Continued**

| Study | Design/population | Smoking status | Health status measure | Outcomes/findings | Comments |
|---|---|---|---|---|---|
| Olufade et al. (1999) | • Cross-sectional study conducted as a pilot test of SCQoL questionnaire<br>• Convenience sample of smokers and former smokers, 18 years of age and older at health clinics<br>• n = 101<br>• 1997–1998<br>• United States | • Current smokers (n = 75)<br>• Former smokers, smokefree for ≥2 weeks (n = 23) | • SF-36<br>• SCQoL | • Compared with current smokers, former smokers had significantly higher scores on physical functioning, vitality, general health, and PCS-36, but they showed no significant differences on other SF-36 measures<br>• Compared with current smokers, former smokers had significantly higher scores on SCQoL measures of self-control, sleep, and anxiety, but they did not differ on social interactions or cognitive functioning<br>• SF-36, mean difference (former smoker vs. current smoker) by QoL dimension:<br>– Physical functioning: 15.7, $p < 0.05$<br>– Role-physical: 13.5, $p > 0.05$<br>– Role-emotional: 11.3, $p > 0.05$<br>– Vitality: 15.1, $p < 0.05$<br>– Mental health: 7.4, $p > 0.05$<br>– Social functioning: 5.4, $p > 0.05$<br>– Bodily pain: 2.9, $p > 0.05$<br>– General health: 21.5, $p < 0.01$<br>– PCS-36: 6.1, $p < 0.05$<br>– MCS-36: 3.4, $p > 0.05$<br>• SCQoL, mean difference (former smoker vs. current smoker) by QoL dimension:<br>– Social interactions: 7.9, $p > 0.05$<br>– Self-control: 45.2, $p < 0.01$<br>– Sleep: 15.1, $p < 0.01$<br>– Cognitive functioning: 9.7, $p > 0.05$<br>– Anxiety: 15.2, $p < 0.05$ | — |

**Table 5.1 Continued**

| Study | Design/population | Smoking status | Health status measure | Outcomes/findings | Comments |
|---|---|---|---|---|---|
| Mulder et al. (2001) | • Cross-sectional study<br>• Random sample of the general population, 20–59 years of age without a history of smoking-related chronic diseases<br>• n = 9,660<br>• 1995–1997<br>• The Netherlands | • Never smokers<br>• Ex-smokers<br>• Current smokers | • RAND-36 (adapted from SF-36) | • Ex-smokers reported significantly higher QoL scores than current smokers for all QoL dimensions (p <.05), except for bodily pain<br>• Adjusted mean scores on QoL measures did not differ significantly between never smokers and ex-smokers, except for bodily pain (p <0.0001)<br>• A higher number of years since quitting was associated with higher scores on general health, vitality, mental health, and the MCS<br>• Differences in QoL scores between ex-smokers and current smokers were more pronounced for QoL dimensions reflecting mental health than physical health<br>• No significant trend was observed for time since quitting | — |

**Table 5.1 Continued**

| Study | Design/population | Smoking status | Health status measure | Outcomes/findings | Comments |
|---|---|---|---|---|---|
| Bellido-Casado et al. (2004) | • Cross-sectional study<br>• Representative sample of the general population older than 14 years of age<br>• n = 265<br>• 1997–2000<br>• Spain | • Smokers<br>• Nonsmokers<br>• Former smokers | • SF-36 | • No statistically significant differences by smoking status in measures of physical health (p = 0.682) or emotional health (p = 0.430)<br>• Physical QoL dimensions—mean scores (95% CI):<br>– Physical function:<br>○ Smokers: 86.92 (83.14–90.71)<br>○ Former smokers: 89.09 (84.74–93.44)<br>– Role-emotional:<br>○ Smokers: 86.81 (78.79–94.83)<br>○ Former smokers: 89.57 (80.35–98.79)<br>– Bodily pain:<br>○ Smokers: 68.24 (62.36–74.13)<br>○ Former smokers: 67.22 (60.46–73.99)<br>– General health:<br>○ Smokers: 59.54 (54.72–64.36)<br>○ Former smokers: 61.24 (55.71–66.78)<br>• Emotional QoL dimensions—mean scores (95% CI):<br>– Vitality:<br>○ Smokers: 59.07 (53.32–64.83)<br>○ Former smokers: 63.55 (56.94–70.17)<br>– Social function:<br>○ Smokers: 83.66 (78.10–89.22)<br>○ Former smokers: 88.00 (81.60–94.39)<br>– Role-emotional:<br>○ Smokers: 79.44 (69.01–89.87)<br>○ Former smokers: 84.67 (72.68–96.66)<br>– Mental health:<br>○ Smokers: 71.99 (66.90–77.08)<br>○ Former smokers: 74.33 (68.48–80.18) | Adjusted for age, sex, social class, alcohol consumption, accumulated exposure to tobacco, diurnal sleepiness, number of known risk factors, and BMI |

**Table 5.1 Continued**

| Study | Design/population | Smoking status | Health status measure | Outcomes/findings | Comments |
|---|---|---|---|---|---|
| Mody and Smith (2006) | • Cross-sectional study<br>• Representative sample of noninstitutionalized adults from the 2001 Behavioral Risk Factor Surveillance System<br>• n = 209,031<br>• 2001<br>• United States | • Nonsmokers (n = 108,072)<br>• Current smokers (n = 48,096)<br>• Ex-smokers (n = 52,863) | • HRQoL measured by self-rated health status, number of days of poor physical health, number of days of poor mental health, and number of days of activity limitations | • Compared with ex-smokers, current smokers were (reported as ORs):<br>– 1.48 (95% CI, 1.32–1.65) times as likely to experience ≥14 days of activity limitations in the past 30 days<br>– 1.29 (no CI provided) times as likely to report poor general health<br>– 1.30 (95% CI, 1.19–1.42) times as likely to report ≥14 days of poor physical health<br>– 1.65 (95% CI, 1.50–1.81) times as likely to report ≥14 days of poor mental health | Adjusted for age, sex, race, education level, marital status, annual household income, BMI, and presence of at least one comorbid disease |
| Heikkinen et al. (2008) | • Cross-sectional study<br>• Nationally representative sample of adults, 30 years of age and older<br>• n = 8,028<br>• 2000–2001<br>• Finland | • Never smokers<br>• Daily smokers<br>• Occasional smokers<br>• Ex-smokers (reported not smoking for at least the past month) | • 15-D<br>• Overall QoL was assessed by a single-question measure that captured the respondent's perception and estimation of his or her QoL | • Ex-smokers reported higher scores than daily smokers on most dimensions of QoL<br>• Compared with men who smoked daily, men who were ex-smokers scored significantly higher in mobility, seeing, breathing, usual activities, discomfort and symptoms, depression, distress, and vitality ($p <.05$) and significantly lower in excreting ($p <0.05$)<br>• Compared with women who smoked daily, women who were ex-smokers scored significantly higher on breathing, eating, depression, distress, and vitality ($p <0.05$) | Adjusted for age |

**Table 5.1 Continued**

| Study | Design/population | Smoking status | Health status measure | Outcomes/findings | Comments |
|---|---|---|---|---|---|
| McClave et al. (2009) (continues on next page) | • Cross-sectional study<br>• Representative sample of noninstitutionalized adults from the 2006 Behavioral Risk Factor Surveillance System surveys in Delaware, Hawaii, Rhode Island, and New York<br>• n = 17,800<br>• United States | • Never smokers (n = 9,149)<br>• Former smokers (n = 5,522)<br>• Nonquitters (n = 1,363)<br>• Unsuccessful quitters (n = 1,766) | • CDC HRQoL-14 Healthy Days Symptoms Module<br>• Self-rated general health status<br>• Life dissatisfaction | • Former smokers were less likely than nonquitters to report life dissatisfaction and frequent depressive symptoms<br>• No significant differences were found in general health status, frequent anxiety symptoms, frequent mental distress, frequent physical distress, frequent activity limitations, frequent pain, infrequent vitality, and frequent sleep impairment<br>• Among men, no significant differences in HRQoL were found between former smokers and nonquitters<br>• Among women, unsuccessful quitters were more likely than current smokers to report the frequent occurrence of mental distress, physical distress, and pain ($p < .05$)<br>• OR (95% CI) by QoL dimension and smoking status:<br>– Fair/poor general health:<br>○ Former smoker: 1.1 (0.7–1.7)<br>○ Never smoker: 1.1 (0.7–1.7)<br>– Life dissatisfaction:<br>○ Former smoker: 0.5 (0.3–0.9)<br>○ Never smoker: 0.4 (0.2–0.7)<br>– Frequent anxiety symptoms:<br>○ Former smoker: 0.7 (0.5–1.1)<br>○ Never smoker: 0.5 (0.4–0.7)<br>– Frequent depressive symptoms:<br>○ Former smoker: 0.7 (0.4–1.0)<br>○ Never smoker: 0.6 (0.4–1.0)<br>– Frequent mental distress:<br>○ Former smoker: 1.3 (0.8–2.0)<br>○ Never smoker: 0.8 (0.5–1.3)<br>– Frequent physical distress:<br>○ Former smoker: 1.3 (0.8–2.0)<br>○ Never smoker: 1.0 (0.6–1.5) | Adjusted for age, race/ethnicity, sex, education, marital status, employment status, chronic disease, and healthcare coverage; unsuccessful quitters were respondents who had smoked at least 100 cigarettes in their lifetime, currently smoked every day or some days, and had abstained from smoking for 1 day or longer during the previous year in an unsuccessful attempt to quit smoking; and nonquitters were current smokers who made no attempt to quit |

**Table 5.1 Continued**

| Study | Design/population | Smoking status | Health status measure | Outcomes/findings | Comments |
|---|---|---|---|---|---|
| (continued from previous page) McClave et al. (2009) | — | — | — | – Frequent activity limitations:<br>○ Former smoker: 1.2 (0.7–2.1)<br>○ Never smoker: 0.8 (0.5–1.4)<br>– Frequent pain:<br>○ Former smoker: 1.3 (0.8–1.9)<br>○ Never smoker: 1.0 (0.7–1.4)<br>– Infrequent vitality:<br>○ Former smoker: 1.1 (0.8–1.5)<br>○ Never smoker: 1.1 (0.8–1.4)<br>– Frequent sleep impairment:<br>○ Former smoker: 0.8 (0.6–1.1)<br>○ Never smoker: 0.6 (0.4–0.8) | — |

*Notes:* **15-D =** 15 dimensions (generic, self-administered measure of HRQoL); **BMI =** body mass index; **CDC =** Centers for Disease Control and Prevention; **CI =** confidence interval; **EuroQoL =** European quality of life; **HRQoL =** health-related quality of life; **MCS =** Mental Component Summary; **OR =** odds ratio; **PCS =** Physical Component Summary; **QoL =** quality of life; **SCQoL =** Smoking Cessation Quality of Life; **SF =** Short Form (survey).

**Table 5.2 Prospective studies about smoking status and quality of life**

| Study | Design/population | Smoking status | Health status measure | Outcomes/findings | Comments |
|---|---|---|---|---|---|
| Stewart et al. (1995) | • Cohort study from RCT of smoking cessation<br>• Current smokers, 18–65 years of age at the time of enrollment into RCT, randomly selected in California and abstinent for 24 hours at baseline<br>• n = 323<br>• United States<br>• HRQoL follow-up at 6 months; smoking status assessed at 3 and 6 months | • Smokers: Had smoked within the last 7 days (n = 220)<br>• Nonsmokers: Had not smoked within the past 7 days; confirmed with cotinine test (n = 103) | • Mental health:<br>– Psychological well-being/distress<br>– Depression/ behavioral-emotional control<br>– Anxiety<br>– Positive affect<br>– Cognitive functioning<br>– Energy/fatigue<br>– Sleep adequacy<br>– Self-esteem<br>– Sense of mastery<br>• Physical health:<br>– Physical functioning<br>– Role functioning<br>– Social functioning<br>– Pain<br>– Current health perceptions | • Compared with smokers at 6 months, nonsmokers had:<br>• Significantly higher scores on mental health dimensions<br>• Significantly lower scores on physical and role functioning<br>• No difference in scores on physical functioning, social functioning, pain, and current health perceptions<br>• Mean difference (smokers vs. nonsmokers) at 6 months by QoL component and dimension:<br>– Mental health:<br>○ Psychological well-being/distress: 4.4, p <.05<br>○ Depression/behavioral–emotional control: 4.9, p <.01<br>○ Anxiety: 7.7, p <.001<br>○ Positive affect: 4.2, p <.05<br>○ Cognitive functioning: 3.4, p <.05<br>○ Energy/fatigue: 6.6, p <.01<br>○ Sleep adequacy: 6.5, p <.05<br>○ Self-esteem: 3.6, p <.05<br>○ Sense of mastery: 9.3, p <.001<br>– Physical health:<br>○ Physical functioning: 0.8, p >.05<br>○ Role functioning: -6.0, p <.05<br>○ Social functioning: -0.7, p >.05<br>○ Pain: 3.4, p >.05<br>○ Current health perceptions: 3.2, p >.05 | For all QoL dimensions, except sleep adequacy, self-esteem, and sense of mastery, adjusted for age, sex, ethnicity, education, employment status, marital status, number of chronic conditions, number of cigarettes smoked at enrollment, nicotine dependence at enrollment, nicotine gum intervention, and initial assessment of HRQoL; and for sleep adequacy, self-esteem, and sense of mastery dimensions, adjusted for all except initial assessment of HRQoL; excluded those who had relapsed at 3 months but quit again by months and those who were not smoking at 3 months but were smoking at 6 months |

**Table 5.2 Continued**

| Study | Design/population | Smoking status | Health status measure | Outcomes/findings | Comments |
|---|---|---|---|---|---|
| Erickson et al. (2004) | • Short-term longitudinal cohort study<br>• Adults actively attempting to quit smoking<br>• n = 34<br>• 1999–2002<br>• United States<br>• Follow-up at 1 week after quitting | • Low addiction: FTND ≤6 (n = 22)<br>• High addiction: FTND >6 (n = 12) | • SCQoL questionnaire:<br>– HRQoL<br>– SF-36<br>• WPS | • Anxiety and cognitive functioning dimensions were significantly worse 1 week after quitting<br>• Self-control dimension improved significantly 1 week after quitting<br>• SF-36 measure of general health showed a significant improvement 1 week after quitting.<br>• WPS score was lower 1 week after quitting but was not significant<br>• Low-addiction group had higher HRQoL at baseline<br>• Compared with the high-addiction group, the low-addiction group showed a significant improvement in more HRQoL domain scores after quitting<br>• SCQoL results by domain:<br>– Anxiety: p = 0.04<br>– Cognitive function: p = 0.02<br>– Self-control: p = 0.001<br>– Sleep: p = 0.15<br>– Social interaction: p = 0.34<br>• SF-36 results by domain:<br>– Bodily pain: p = 0.12<br>– General health: p = 0.01<br>– Mental health: p = 0.14<br>– Physical function: p = 0.27<br>– Role-emotional: p = 0.65<br>– Role-physical: p = 0.25<br>– Social function: p = 0.26<br>– Vitality: p = 0.53<br>• WPS: p = 0.17 | — |

**Table 5.2 Continued**

| Study | Design/population | Smoking status | Health status measure | Outcomes/findings | Comments |
|---|---|---|---|---|---|
| Gutiérrez-Bedmar et al. (2009) | • Cohort study<br>• University graduates<br>• n = 5,234<br>• 1999–2006<br>• Spain<br>• Follow-up at 4 years | • Baseline:<br>– Nonsmokers (n = 2,639)<br>– Ex-smokers (n = 1,419)<br>– Smokers (n = 1,048)<br>• Follow-up:<br>– Nonsmokers (n = 3,594)<br>– Smokers (n = 818)<br>– Recent quitters (n = 435)<br>– Starters (n = 205) | • SF-36 (validated Spanish version) | • Ex-smokers had significantly lower mean scores on the SF-36 than nonsmokers in two QoL dimensions: role-physical and bodily pain<br>• Ex-smokers had significantly higher scores than smokers of 15–24 cigarettes per day in two QoL dimensions: general health and role-emotional<br>• Ex-smokers had significantly higher scores than smokers of ≥25 cigarettes per day in four QoL dimensions: general health, social<br>• functioning, role-emotional, and mental health<br>• At follow-up, the recent quitters group had significantly better mean scores than smokers in two QoL dimensions: general health and role-emotional | Adjusted for age and sex |
| Tian et al. (2016) | • Cohort study<br>• 25-year follow-up of participants in a previous cohort, 23–34 years of age at enrollment<br>• n = 2,080<br>• 2001–2011<br>• Australia<br>• Follow-up at 2 and 5 years | • Baseline smoking status:<br>– Never smoker<br>– Former smoker<br>– Current smoker<br>• Change in smoking status:<br>– Stable, never smokers<br>– Stable, former smokers<br>– Resumed<br>– Continuing<br>– Quitter | • SF-12 PCS and MCS | • No significant differences in HRQoL dimensions at baseline between never and former smokers.<br>• Continuing smokers had larger reductions than quitters<br>• The risk of clinically significant improvement in physical HRQoL was higher for quitters than for continuing smokers<br>• Clinically meaningful improvement in PCS (quitters vs. continuing): RR = 1.43 (95% CI, 1.03–1.98)<br>• Mean difference, baseline PCS (former smokers vs. never smokers): -0.49 (95% CI, -1.32–0.34)<br>• Mean difference, baseline MCS (former smokers vs. never smokers): -0.36 (95% CI, -1.31–0.60) | Adjusted for age, sex, marital status, follow-up duration, baseline PCS, residing in a major city, education level, BMI, IPAQ level, total alcoholic drinks per day, and diagnosis of current severe psychological distress |

*Notes:* **BMI =** body mass index; **CI =** confidence interval; **FTND =** Fagerström Test for Nicotine Dependence; **HRQoL =** health-related quality of life; **IPAQ =** International Physical Activity Questionnaire; **MCS =** Mental Component Summary; **PCS =** Physical Component Summary; **QoL =** quality of life; **RCT =** randomized controlled trial; **RR =** relative risk; **SCQoL =** Smoking Cessation Quality of Life; **SF =** Short Form (survey); **WPS =** Work Performance Scale.

**Table 5.3 Prospective studies of populations undergoing cessation treatment**

| Study | Design/population | Smoking status | Health status measure | Outcomes/findings | Comments |
|---|---|---|---|---|---|
| Bolliger et al. (2002) | • Cohort study from RCT of oral nicotine inhaler for smoking reduction<br>• Healthy adult volunteers, unable or unwilling to stop smoking immediately, randomized to active or placebo inhalers for 18 months and encouraged to reduce smoking as much as possible<br>• n = 400<br>• Switzerland<br>• Follow-up for 24 months | • Successful reducers: Reduction of daily cigarettes of at least 50% from week 6 to month 24 (n = 25)<br>• Control group: Failed to reduce smoking or carbon monoxide output, or failed to attend one or more of seven follow-up visits (n = 285) | • SF-36: General health, physical functioning, energy, and emotional well-being | • Significantly greater improvement in general health was seen in successful reducers compared with those in the control group<br>• Among successful reducers, physical functioning showed nonsignificant *t* trend toward greater improvement<br>• Emotional well-being and energy improved more in the successful reducers than among those in the control group, but the difference was not significant<br>• Mean change from baseline by QoL dimension and smoking status:<br>– General health:<br>○ Successful reducer: 9.4<br>○ Control group: 2.3<br>○ p = 0.049<br>– Physical functioning:<br>○ Successful reducer: 7.4<br>○ Control group: 4.9<br>○ p = 0.073<br>– Energy:<br>○ Successful reducer: 6.8<br>○ Control group: 5.3<br>○ p = 0.23<br>– Emotional well-being:<br>○ Successful reducer: 6.2<br>○ Control group: 4.2<br>○ p = 0.50 | — |

**Table 5.3 Continued**

| Study | Design/population | Smoking status | Health status measure | Outcomes/findings | Comments |
|---|---|---|---|---|---|
| Zillich et al. (2002) | • Cohort study<br>• Adult smokers interested in quitting and enrolled in a pharmacist-based smoking cessation program<br>• n = 31<br>• 2000–2001<br>• United States<br>• Follow-up at<br>• 6 months | • Smoker<br>• Abstinent: Self-reported abstinence during the previous 7 days confirmed with exhaled carbon monoxide test | • SCQoL questionnaire | • Among those who reported abstinence, there were statistically significant improvements for vitality, mental health, and self-control at 3 months ($p < .05$) | SCQoL missing for those who did not report abstinence |
| Croghan et al. (2005) | • Cohort study<br>• Patients undergoing treatment for nicotine independence<br>• n = 206<br>• 1998<br>• United States<br>• Follow-up for 1 year | • Abstinent ≤6 days (n = 60)<br>• Continuously abstinent for entire year (n = 146) | • SF-36 | • Compared with those who were not continuously abstinent for a year, those who were continuously abstinent for a year reported significantly improved MCS, role limitations-emotional, role limitations-physical, and general health | Controlled for scores at baseline; mean scores not reported |
| Rungruanghiranya et al. (2008) | • Placebo-controlled RCT for effectiveness of nicotine gum<br>• n = 43<br>• Thailand<br>• Follow-up at<br>• 3 months | • Abstinence failure (n = 31)<br>• Abstinence successful: Complete and continuous abstinence for 3 months (n = 12) | • WHOQoL-BREF | • No significant differences in QoL scores were observed between those who successfully quit and those who failed | — |

**Table 5.3 Continued**

| Study | Design/population | Smoking status | Health status measure | Outcomes/findings | Comments |
|---|---|---|---|---|---|
| Hays et al. (2012) | • Placebo-controlled RCT ofvarenicline and bupropion sustained release<br>• Adults who had smoked ≥10 cigarettes per day for the past year<br>• n = 2,052<br>• 2003–2005<br>• United States<br>• Follow-up for 1 year | • Adults who had smoked<br>• ≥10 cigarettes per day for the past year | • SCQoL | • Both treatment groups showed clinically relevant differences in health transition and self-control at 1 year<br>• Those with longer periods of abstinence reported better health transition, self-control, vitality, smoking-related anxiety, and MCS than those with shorter periods of abstinence | — |
| Piper et al. (2012) | • Cohort study from RCT of smoking cessation treatments<br>• n = 1,504<br>• 2005–2007<br>• United States<br>• Follow-up for 3 years | • Non-quitter<br>• Quitter: 7-day point prevalence confirmed with carbon monoxide test | • QoL Inventory | • Compared with nonquitters, quitters reported significantly lower QoL scores at years 1 and 3<br>• Compared with continuing smokers, quitters showed improved global QoL, HRQoL, and affect at years 1 and 3 and fewer stressors by year 3 | — |

*Notes:* **MCS =** Mental Component Summary; **QoL =** quality of life; **RCT =** randomized controlled trial; **SCQoL =** Smoking Cessation Quality of Life; **SF =** Short Form (survey); **WHOQoL-BREF =** World Health Organization Quality of Life-BREF.

**Table 5.4 Prospective studies of special populations**

| Study | Design/population | Smoking status | Health status measure | Outcomes/findings | Comments |
|---|---|---|---|---|---|
| Taira et al. (2000) | • Cohort study of RCT of atherectomy techniques<br>• Patients who underwent percutaneous coronary revascularization for coronary artery disease<br>• n = 1,432<br>• United States<br>• Follow-up for 1 year | • Nonsmokers<br>• Persistent smokers<br>• Quitters | • SF-36 | • All groups showed improvement on dimensions of the SF-36, but persistent smokers showed a smaller improvement than nonsmokers across all dimensions<br>• Quitters showed improvement equal to or better than nonsmokers across all dimensions<br>• Persistent smokers showed significantly less improvement than quitters in three QoL dimensions: physical functioning, social functioning, and mental health<br>• Mean difference by QoL dimension and follow-up period:<br>– Physical functioning:<br>○ 6 months: 8.4 ($p < 0.001$)<br>○ 1 year: 5.8 ($p = 0.01$)<br>– Role-physical:<br>○ 6 months: 10.3 ($p < 0.001$)<br>○ 1 year: 6.2 ($p = 0.14$)<br>– Bodily pain:<br>○ 6 months: 4.2 ($p < 0.001$)<br>○ 1 year: 2.9 ($p = 0.25$)<br>– General health:<br>○ 6 months: 5.5 ($p = 0.001$)<br>○ 1 year: 4.0 ($p = 0.07$)<br>– Vitality:<br>○ 6 months: 5.2 ($p < 0.001$)<br>○ 1 year: 2.7 ($p = 0.25$)<br>– Social functioning:<br>○ 6 months: 7.5 ($p < 0.001$)<br>○ 1 year: 6.0 ($p = 0.01$)<br>– Role-emotional:<br>○ 6 months: 3.7 ($p = 0.039$)<br>○ 1 year: 0.1 ($p = 0.92$)<br>– Mental health:<br>○ 6 months: 3.7 ($p < 0.001$)<br>○ 1 year: 3.8 ($p = 0.05$) | Adjusted for demographic and clinical characteristics, comorbid conditions, and baseline health status |

**Table 5.4 Continued**

| Study | Design/population | Smoking status | Health status measure | Outcomes/findings | Comments |
|---|---|---|---|---|---|
| Mitra et al. (2004) | • Longitudinal survey of adults with disabilities (Massachusetts Survey of Secondary Conditions)<br>• n = 355<br>• 1996–2000<br>• Massachusetts | • Nonsmokers<br>• Smokers<br>• Quitters<br>• Starters | • SF-36 (enabled version) | • Compared with smokers, quitters experienced<br>• significantly more improvement in mental health, energy and vitality, and general health perception | Adjusted for sex, race/ethnicity, years of education, age at baseline, number of QoL dimensions on which respondents were dependent on activities of daily living |
| Wiggers et al. (2006) | • RCT of nicotine replacement therapy and behavioral intervention<br>• Patients with symptomatic atherosclerotic disease<br>• n = 344<br>• The Netherlands<br>• Follow-up for 1 year | • Smokers with a failed quit attempt<br>• Smokers without a failed quit attempt<br>• Quitters | • SF-36<br>• Aquarel<br>• VascuQoL | • Study found no effects of smoking status on QoL | — |
| Jensen et al. (2007) | • Longitudinal cohort study<br>• Patients after radical radiotherapy or surgery for head and neck cancer<br>• n = 114<br>• Denmark | • Never smokers<br>• Smokers<br>• Quitters | • EORTC-C30<br>• EORTC-H&N35 | • Compared with smokers, those who had quit smoking at follow-up showed higher physical and mental functioning<br>• The QoL scores of quitters fell between those of never smokers and smokers | — |

**Table 5.4 Continued**

| Study | Design/population | Smoking status | Health status measure | Outcomes/findings | Comments |
|---|---|---|---|---|---|
| Balduyck et al. (2011) | • Cohort study<br>• Patients undergoing non-small-cell lung cancer surgery<br>• n = 70<br>• Belgium<br>• Follow-up for 12 months | • Nonsmokers<br>• Former smokers (stopped smoking before diagnosis of lung cancer)<br>• Recent quitters (patients who stopped smoking between diagnosis and surgery) | • EORTC-C30<br>• EORTC-LC13 | • All groups had a reduction in QoL after surgery, but those who were former smokers at baseline and those who quit smoking after diagnosis showed improved QoL scores at follow-up compared with those who continued smoking | — |
| Papadopoulos et al. (2011) | • Longitudinal cohort study<br>• Patients with COPD who smoked and were recommended to quit smoking<br>• Greece<br>• n = 26<br>• Follow-up for 2 months | • Smokers<br>• Quitters | • SF-12<br>• CCQ | • Those who successfully quit smoking for 2 months showed significant differences in all domains of the SF-12 and in total CCQ score from baseline<br>• CCQ total score:<br>– Before: 1.08 ± 0.82<br>– Follow-up: 0.72 ± 0.69<br>– p <0.001 | — |

*Notes:* **CCQ =** Clinical COPD Questionnaire; **COPD =** chronic obstructive pulmonary disease; **EORTC-C30 =** European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, Core Module; **EORTC-H&N35 =** European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, Head and Neck Module; **EORTC-LC13 =** European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, Lung Cancer Module; **QoL =** quality of life; **RCT =** randomized controlled trial; **SF =** Short Form (survey); **VascuQoL =** Vascular Quality of Life (questionnaire).

All of the studies determined whether participants were former smokers, but the period of abstinence from smoking required for classification as a former smoker was not uniform across studies, and some studies did not specify a minimum time period of abstinence (McClave et al. 2009; Tian et al. 2016). Some studies confirmed smoking status by a biomarker, such as cotinine (Stewart et al. 1995) or carbon monoxide (Zillich et al. 2002; Rungruanghiranya et al. 2008; Hays et al. 2012; Piper et al. 2012). Several studies (Stewart et al. 1995; Croghan et al. 2005; Wiggers et al. 2006; Piper et al. 2012) defined abstinence as a period of 7 days without smoking, but others used different standards, including 2 weeks (Olufade et al. 1999), 1 month (Mitra et al. 2004; Heikkinen et al. 2008), 3 months (Rungruanghiranya et al. 2008), and 5 years (Tillmann and Silcock 1997). One study, Erickson and colleagues (2004), considered level of addiction and divided former smokers into subgroups of low and high addiction, as assessed by the Fagerström Test for Nicotine Dependence (FTND) (Heatherton et al. 1991).

Some variation was also observed with regard to comparison groups used across studies. For example, as the reference group for comparing outcomes among those who had quit successfully, McClave and colleagues (2009) used unsuccessful quitters, defined as those who had attempted to quit at least once in the past year but were currently smoking. In a clinical trial of nicotine replacement therapy (NRT), Bolliger and colleagues (2002) compared successful reducers, who were ongoing smokers who had achieved at least a 50% reduction in the number of cigarettes smoked daily from week 6 to month 24 of the trial, with unsuccessful reducers.

## Epidemiologic Evidence

### Cross-Sectional Studies

Table 5.1 summarizes cross-sectional studies of smoking cessation and morbidity. Seven cross-sectional studies assessed smoking cessation and morbidity by asking participants to self-report smoking status and a measure of morbidity at the time of survey. Several studies that used the SF-36 to assess HRQoL observed that having quit smoking was associated with higher scores on some measures. Tillmann and Silcock (1997), in a study of 3,000 participants, reported significantly higher HRQoL, as measured by SF-36 and EuroQoL tariff scores, among former smokers who had smoked 5 years or more compared with current smokers in Scotland. Olufade and colleagues (1999), in a sample of 101 adults, reported that former smokers (smokefree for 2 or more weeks) had significantly higher scores on physical functioning, vitality, general health, and the Physical Component Summary compared with current smokers; however, they found no significant differences for other measures on the SF-36. In the Netherlands, Mulder and colleagues (2001) reported significantly higher HRQoL scores for former smokers on all measures of the SF-36, except bodily pain compared with current smokers. In their sample, the HRQoL of former smokers approached that of never smokers, and adjusted mean scores on measures of the SF-36 did not differ significantly between never smokers and former smokers, except for bodily pain. Mulder and colleagues (2001) also found that increasing years since quitting was associated with higher scores on general health, vitality, mental health, and the Mental Component Summary. These researchers noted that overall differences in QoL between former smokers and current smokers were more pronounced for measures of mental health than for physical health. Although the first three studies found various differences by smoking status using the SF-36, in a representative sample of adults older than 14 years of age in Spain, Bellido-Casado and colleagues (2004) found no differences by smoking status in measures of physical, emotional, or mental health in the SF-36.

Two studies used data from the Behavioral Risk Factor Surveillance System (BRFSS), a telephone-based survey of U.S. adults 18 years of age and older. In an analysis of data from 2001 from a representative sample of 209,031 adults, Mody and Smith (2006) found that, compared with nonsmokers and former smokers, current cigarette smokers were more likely to experience (in the past 30 days) 14 or more days of activity limitation, 14 or more days of poor physical health, and 14 or more days of poor mental health. In addition, in their comparisons with former smokers, they found that current smokers were more likely to report poor general health. McClave and colleagues (2009), who used BRFSS data from 2006 in four states, found that former smokers and nonsmokers were less likely than current smokers (nonquitters) to report life dissatisfaction and frequent depressive symptoms; however, there were no significant differences between current and former smokers in reported general health status, frequent anxiety symptoms, frequent mental distress, frequent physical distress, frequent activity limitations, frequent pain, infrequent vitality, or frequent sleep impairment. Among men, there were no significant differences in HRQoL between former and current smokers. Among women, reported frequent mental and physical distress did not differ significantly between former and never smokers and current smokers, but among current smokers, women who tried to quit smoking and failed were more likely to report frequent mental stress and physical distress than were women who did not try to quit.

Heikkinen and colleagues (2008) used the 15-D instrument to assess HRQoL in a nationally representative sample of about 8,000 adults 30 years of age and older in Finland. Compared with daily smokers, former smokers (defined as those who had not smoked for at least the past month) reported higher scores on most measures of the instrument.

## Longitudinal Studies

Tables 5.2–5.4 summarize findings from 16 longitudinal studies of smoking cessation and general morbidity. These studies fall into three categories: (1) prospective cohort studies, (2) randomized controlled trials (RCTs), and (3) observational studies embedded within RCTs in which the data from the RCTs were analyzed as though the studies were observational without preservation of the randomization. With these types of longitudinal designs, smoking status is assessed before the outcome occurs. In contrast, cross-sectional studies assess smoking status and the outcome at the same point in time. Prospective studies were considered for quality of life (Table 5.2), populations receiving cessation treatment (Table 5.3), and populations with specific medical conditions (Table 5.4). Studies included in Table 5.2 were all designed as prospective cohorts (Stewart et al. 1995; Erickson et al. 2004; Gutiérrez-Bedmar et al. 2009; Tian et al. 2016). Table 5.3 includes studies with different longitudinal designs: prospective cohort (Zillich et al. 2002; Croghan et al. 2005), RCT (Rungruanghiranya et al. 2008; Hays et al. 2012), and observational study within an RCT (Bolliger et al. 2002; Piper et al. 2012). Table 5.4 includes longitudinal studies designed as prospective cohorts (Taira et al. 2000; Mitra et al. 2004; Jensen et al. 2007; Balduyck et al. 2011; Papadopoulos et al. 2011) or observational studies within an RCT (Wiggers et al. 2006).

### *Longitudinal Studies of General Populations*

At the 4-year follow-up of 5,234 participants of a study based in Spain, Gutiérrez-Bedmar and colleagues (2009) found that compared with current smokers, mean scores for general, emotional, and mental health were significantly better among recent former smokers who had quit after the baseline assessment and before the 4-year follow-up. Tian and colleagues (2016) assessed HRQoL, using the SF-12, in relation to smoking status at baseline (never, former, and current smokers) and after 5 years of follow-up in about 2,000 Australian adults 31–41 years of age at follow-up. There were no significant differences in measures comparing never and former smokers at baseline, but at the 5-year follow-up, those who had continued to smoke had larger reductions in QoL scores than those who reported being former smokers at follow-up and were smokers at baseline. For these quitters, the estimated relative risk for a clinically significant improvement in physical HRQoL scores was higher compared with continuing smokers. Additionally, former smokers had a higher likelihood of a clinically significant improvement in emotional and mental health HRQoL scores compared with continuing smokers.

### *Longitudinal Studies of Populations Undergoing Cessation Treatment*

Eight trials considered participants engaged in cessation treatment. In one, Stewart and colleagues (1995) assessed the smoking status of 323 adults enrolled in a community-based RCT of smoking cessation. At baseline, all participants were smokers. At 6 months, quitters had a significantly higher score on all assessed measures of mental health compared with continuing smokers, including psychological well-being, anxiety, positive affect, cognitive functioning, energy, sleep adequacy, self-esteem, and sense of mastery. In contrast, for the five measures of physical health, there were no statistically significant differences between the groups on four measures: physical functioning, social functioning, pain, and current health perceptions.

Zillich and colleagues (2002) used the SCQoL questionnaire to evaluate changes in HRQoL among 31 participants in a nonrandomized, unblinded trial to evaluate the effectiveness of a pharmacist-based smoking cessation program. Vitality, mental health, and self-control improved significantly among those who successfully quit over the 6 months of follow-up compared with baseline. However, data were missing for participants who did not successfully quit and did not return for follow-up. In Switzerland, Bolliger and colleagues (2002) enrolled a cohort of 400 participants from an earlier RCT of an oral nicotine inhaler for smoking reduction and examined QoL in relation to smoking reduction. Healthy adult volunteers were randomized to active or placebo inhalers and encouraged to reduce their smoking as much as possible; the cohort was followed for 24 months. The comparison group of nonreducers (less than a 50% reduction in the number of cigarettes smoked daily from week 6 to month 24) was used for comparison with successful reducers (at least a 50% reduction). Compared with the control group, successful reducers had significantly greater improvement in general health, as measured by the SF-36.

Among those who quit in a study of 34 smokers, Erickson and colleagues (2004) considered whether low (FTND score ≤6) or high (FTND score >6) levels of addiction affected QoL 1 week after the quit date. The lower addiction group showed a significant improvement in more of the HRQoL domain scores after the quit date compared with the higher addiction group.

Croghan and colleagues (2005) evaluated 206 patients treated for nicotine dependence for changes in their health status, as measured by the SF-36, 1 year after consultation at the Mayo Clinic. Patients who stopped smoking for 1 year or more had significantly higher QoL measures at baseline compared with a demographically similar group who had not stopped smoking. After controlling for baseline scores, patients who stopped smoking for 1 year or more had significantly improved scores on the Mental Component Summary and for role limitations, both emotional and physical, and significantly improved general health compared with those who were not abstinent for a year.

Rungruanghiranya and colleagues (2008) performed a placebo-controlled RCT in Thailand that considered the effectiveness of nicotine gum for cessation and examined changes in QoL after 3 months. Forty-six subjects underwent screening for the study; two were excluded because of NRT use, and one was excluded due to a recent diagnosis of diabetes. Among the 43 participants, the study revealed no significant differences in improved QoL between those who had successfully quit smoking and those who had not.

Piper and colleagues (2012) assessed QoL in 1,504 participants making a quit attempt as part of an RCT of smoking cessation. Both former smokers (i.e., quitters) and current smokers (nonquitters) experienced a reduction in global QoL at the 1- and 3-year follow-ups, but former smokers had a significantly smaller decrease in global QoL. Former smokers showed slight improvement in HRQoL at years 1 and 3, an outcome significantly different from the decreases in HRQoL reported by continuing smokers. Former smokers also reported a decrease in negative affect at 1 year, which differed significantly from the slight increase in continuing smokers.

Hays and colleagues (2012) implemented a placebo-controlled RCT in which 2,052 participants were treated with varenicline, bupropion SR (sustained release), or placebo and followed for 52 weeks. Participants in both treatment groups showed clinically relevant differences in health transition (perceived health compared with baseline) and self-control at follow-up compared with participants in the placebo group at follow-up. In terms of abstinence, those who had a longer period of abstinence reported better health transition and self-control at follow-up compared with those who were abstinent for a shorter period. Among those with a longer period of abstinence, findings were similar to those abstinent for a shorter period of time for vitality, smoking-related anxiety, and improvement in scores on the Mental Component Summary.

### Longitudinal Studies of Special Populations

Table 5.4 summarizes six longitudinal studies that considered smoking cessation in special populations defined by disease status. Taira and colleagues (2000) assessed QoL after percutaneous coronary revascularization in 1,432 patients with coronary artery disease within two RCTs (Baim et al. 1998, 2001). All groups (nonsmokers, former smokers [quitters], and persistent smokers) showed improvements on measures of the SF-3, but the extent of improvement differed by smoking status. At 6 months, after controlling for baseline scores on the SF-36, improvement among former smokers was comparable to that of nonsmokers. At 1 year, persistent smokers continued to show significantly less improvement than former smokers in physical functioning, social functioning, and mental health. Compared with continuing smokers, former smokers made significantly greater gains in both Physical Component Summary and Mental Component Summary scores at 6 months and 1 year.

Using data from Wilber and colleagues (2002), Mitra and colleagues (2004) performed a longitudinal study of 355 adults with disabilities and found that changes in smoking status were associated with future changes in QoL scores—with former smokers experiencing significantly more improvement in mental health, energy and vitality, and perceived general health compared with current smokers. In the Netherlands, Wiggers and colleagues (2006) studied 344 smokers with atherosclerotic vascular disease who were participating in an RCT of NRT combined with a behavioral intervention, and considered both general (SF-36) and disease-specific QoL (Aquarel and VascuQoL). Overall, participants showed improved physical and mental QoL, as measured by SF-36 at follow-up (2, 6, and 12 months), but there were no differences by smoking status. In a study based in Denmark, Jensen and colleagues (2007) considered smoking status and QoL in 114 patients surveyed after treatment for head and neck cancer. Those who had quit smoking at postsurgical follow-up showed higher physical and mental functioning compared with continuing smokers.

In Greece, Papadopoulos and colleagues (2011) investigated smoking cessation and QoL using a disease-specific score (the Clinical COPD Questionnaire [CCQ]) in a cohort of 26 participants with chronic obstructive pulmonary disease who had successfully quit smoking for 2 months. QoL, as measured by both the CCQ and a generic scale (SF-12), improved after 2 months of cessation. Finally, Balduyck and colleagues (2011), in a study based in Belgium, considered 70 patients' return-to-baseline QoL after surgery for lung cancer using a disease-specific score (EORTC-C30 and EORTC-LC13) that was administered after a reduction in smoking following surgery in all three smoking status groups (current smoker, former smokers, and recent quitters). Those who were former smokers at baseline (i.e., before their diagnosis) and those who quit smoking after diagnosis both showed improved QoL at follow-up compared with those who continued to smoke, although those who were former smokers at baseline had a faster return to baseline QoL than recent quitters.

## Synthesis of the Evidence

Studies of morbidity and smoking cessation vary in their definitions of cessation, length of follow-up, and morbidity measures, including QoL. Nonetheless, despite these variations, the overall findings indicate that smoking cessation lessens general morbidity, specifically as measured by HRQoL and assessments of health status. Although the level of HRQoL for former cigarette smokers is between that of current smokers and never smokers, the HRQoL of former smokers approaches that of never smokers for many measures. This pattern is found in samples of the general population, in study participants undergoing cessation treatment, and in persons with specific diseases. Moreover, greater benefits have been found for measures of mental health than for measures of physical health. Some evidence suggests that persons with lower levels of addiction before cessation appear to experience greater gains in mental health, and those who are abstinent for a longer period show higher levels of improvement in mental health.

One critical factor to consider in interpreting the evidence on smoking cessation and health is the potential for reverse causation—that is, the presence of symptoms or a disease leading to a decision to quit. If that is the case, the rates of symptoms in cross-sectional data might be higher in former smokers than in current smokers. Even in prospective cohort studies, when changes in indicators of health are tracked over time, the causal direction may be difficult to ascertain, particularly if participants quit as symptoms develop or as their well-being declines. Randomized trials of cessation interventions are not subject to such temporal limitations; however, generalizability may be limited because the populations in these studies may not reflect smokers in general.

Temporal ambiguity is a particular concern in cross-sectional studies that assess smoking status and morbidity at the same time. In these cases, a better HRQoL in former smokers than in current smokers may result from smoking cessation or be a contributing factor to successful smoking cessation. Additionally, lower HRQoL may reduce the ability to successfully quit smoking. One further complication in interpreting cross-sectional data is related to the motivation of smokers to quit because of the development of smoking-related symptoms of disease. This type of reverse causation generally tends to reduce associations of cessation with beneficial outcomes.

Longitudinal studies—including prospective cohort studies, RCTs, and observational studies within an RCT—provide higher quality evidence with less opportunity for temporal ambiguity, and they can measure QoL at baseline before differences across groups classified by smoking status are assessed. However, smokers who do not quit may be less likely to remain in longitudinal studies during follow-up (Zillich et al. 2002). Regardless, as with the evidence considered in the 1990 Surgeon General's report on the health benefits of smoking cessation (USDHHS 1990), the variety of measures used in studies of cessation can limit comparability and summarization across studies.

## Summary of the Evidence

This section reviews evidence on smoking cessation and general morbidity using a variety of broad, nonspecific but validated measures, such as QoL indicators and health status and disease-specific measures. For the measures that are broad and nonspecific, the determinants of responses are multifactorial. Thus, some studies reviewed in this chapter attempted to address potential confounding. Based on consistent evidence across the studies reviewed (Tables 5.1 and 5.2), former smokers have less general morbidity than current smokers, as reflected in higher QoL scores and in multiple measures of health status. Confounding may have affected the results of some of the studies reviewed; however, confounding alone does not adequately explain the consistent finding of lower morbidity and higher QoL among former smokers compared with current smokers. Selection bias is also a potential concern if persistent smokers, particularly those who are ill, are less likely than quitters to remain in follow-up during longitudinal studies.

Despite such limitations, the evidence for lower morbidity and higher QoL among former smokers than among current smokers is strengthened by the higher levels of improvement in QoL seen among those who had abstained from smoking longer; such a finding supports a conclusion of causality. Former smokers tend to have higher morbidity than never smokers; and in some subgroups, the morbidity of former smokers can approach that of never smokers, such as among those with lower levels of addiction before cessation.

A causal link between smoking cessation and a decrease in general morbidity is supported by the biologic plausibility of the relationship. Active smoking drives various nonspecific processes of injury (e.g., inflammation), which lessen with the end of exposure to the toxins in tobacco smoke (USDHHS 2010). Because the morbidity measures addressed in the studies reviewed in this chapter are broad and nonspecific, a single mechanism cannot be invoked to explain the association between smoking cessation and reduction of general morbidity. However, many well-supported mechanisms link smoking cessation to improvements in more specific measures of health, such as disease-specific outcomes, thus underscoring the likelihood that those who quit smoking will have lower rates of morbidity.

# Benefits of Smoking Cessation on All-Cause Mortality

Increased all-cause mortality is a well-established causal consequence of smoking (USDHHS 2004, 2014). Chapter 4 of this report (The Health Benefits of Smoking Cessation) summarizes disease risks from smoking and the changes in risk that follow smoking cessation for the major types of chronic diseases. This section briefly summarizes the well-documented and extensive scientific evidence on the health benefits of smoking cessation on all-cause mortality. The review is limited in scope because the topic has been extensively covered in prior reports.

## Conclusions from Previous Surgeon General's Reports

The 1964 Surgeon General's report included a table on all-cause mortality with the findings of seven cohort studies. In a pioneering quantitative synthesis of the data from the seven studies, the ratio of deaths observed to deaths expected was 1.68:1 (USDHEW 1964). A contemporary analysis of the data from the 1964 Surgeon General's report showed statistically significant increases in all-cause mortality in all of the studies (Figures 5.1a and 5.1b) (Schumacher et al. 2014). The 1964 Surgeon General's report concluded that, "Cigarette smoking is associated with a 70 percent increase in the age-specific death rates of males, and to a lesser extent with increased death rates of females. The total number of excess deaths causally related to cigarette smoking in the U.S. population cannot be accurately estimated. In view of the continuing and mounting evidence from many sources, it is the judgment of the [Surgeon General's Advisory Committee on Smoking and Health] that cigarette smoking contributes substantially to mortality from certain specific diseases and to the overall death rate" (USDHEW 1964, p. 31).

By the time of the 1964 report, evidence from five cohort studies showed lower risk for all-cause mortality in former smokers compared with current smokers, and data from several cohorts showed declining risk for death in former smokers, compared with current smokers, as the interval since cessation lengthened.

Subsequent Surgeon Generals' reports (USDHEW 1969, 1979; USDHHS 1989, 1990, 2004, 2014) have comprehensively covered this topic and published findings comparable to those in the 1964 Surgeon General's report. In brief, using data from the American Cancer Society's Cancer Prevention Study II, the 1990 Surgeon General's report included lifetable analyses on the health benefits of smoking cessation, offering the following conclusions on all-cause mortality:

- "Former smokers live longer than continuing smokers, and the benefits of quitting extend to those who quit at older ages. For example, persons who quit smoking before age 50 have one-half the risk of dying in the next 15 years compared with continuing smokers.
- Smoking cessation at all ages reduces the risk of premature death.
- Among former smokers, the decline in risk of death compared with continuing smokers begins shortly after quitting and continues for at least 10 to 15 years. After 10 to 15 years of abstinence, risk of all-cause mortality returns nearly to that of persons who never smoked" (USDHHS 1990, p. 92).

The 2004 Surgeon General's report extended these findings by comprehensively documenting and updating the evidence on active smoking and disease, noting that "fortunately for former smokers, studies show that substantial risks of smoking can be reduced by successfully quitting at any age" (USDHHS 2004, p. 25). Furthermore, the report concluded that "quitting smoking has immediate as well as long-term benefits, reducing risks for disease caused by smoking and improving health in general" (USDHHS 2004, p. 25).

The 2014 Surgeon General's report provided the most recent extensive review of the consequences of smoking on health and confirmed findings from previous reports in the series:

- "The evidence is sufficient to infer that cigarette smoking increases risk for all-cause mortality in men and women.
- The evidence is sufficient to infer that the relative risk of dying from cigarette smoking has increased over the last 50 years in men and women in the United States" (USDHHS 2014, p. 641).

The 2014 Surgeon General's report also compared the relative risks for all-cause mortality in the American Cancer Society's Cancer Prevention Studies I (1959–1965) and II (1982–1988) with those in a pooled analysis of five contemporary cohorts with follow-up through 2010. The

**Figure 5.1a Incidence rate ratios for death from any cause, by smoking status**

| Study | Weight (fixed) % | Weight (random) % | Incidence rate ratio (95% CI) |
|---|---|---|---|
| British doctors | 7.5 | 14.8 | 1.44 (1.32–1.56) |
| Men in 9 states | 19.6 | 18.5 | 1.70 (1.61–1.79) |
| U.S. veterans | 40.2 | 20.1 | 1.79 (1.73–1.86) |
| California occupational | 1.0 | 4.6 | 1.78 (1.41–2.25) |
| California Legion | 1.6 | 6.6 | 1.58 (1.32–1.90) |
| Canadian veterans | 14.6 | 17.6 | 1.65 (1.56–1.76) |
| Men in 25 states | 15.6 | 17.8 | 1.63 (1.54–1.73) |
| Fixed-effects model | 100.0 | — | 1.69 (1.66–1.73) |
| Random-effects model | — | 100.0 | 1.65 (1.56–1.75) |

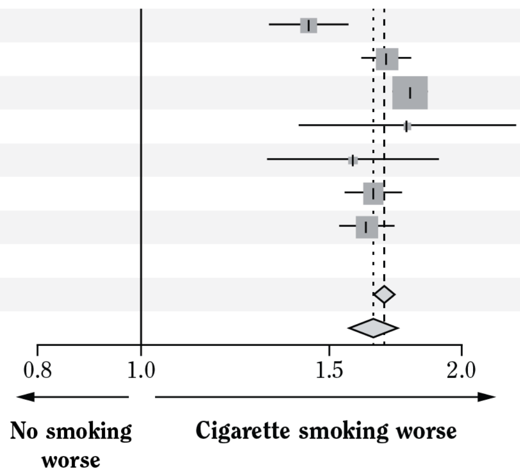
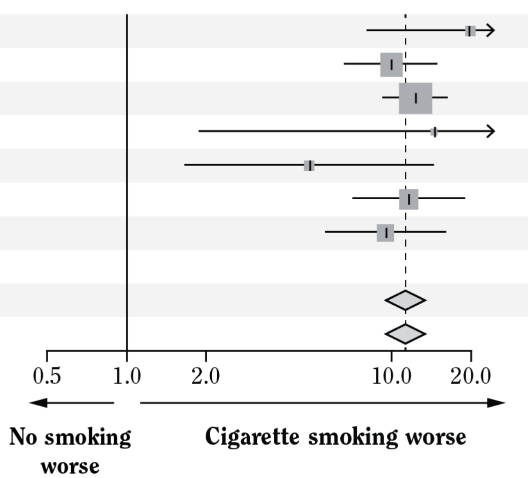



**Figure 5.1b Incidence rate ratios for death from lung cancer, by smoking status**

| Study | Weight (fixed) % | Weight (random) % | Incidence rate ratio (95% CI) |
|---|---|---|---|
| British doctors | 4.2 | 4.2 | 19.86 (8.07–48.85) |
| Men in 9 states | 20.7 | 20.7 | 9.95 (6.64–14.91) |
| U.S. veterans | 44.2 | 44.2 | 12.33 (9.34–16.26) |
| California occupational | 0.8 | 0.8 | 14.50 (1.87–112.27) |
| California Legion | 2.9 | 2.9 | 4.90 (1.66–14.49) |
| Canadian veterans | 14.7 | 14.7 | 11.65 (7.20–18.84) |
| Men in 25 states | 12.6 | 12.6 | 9.54 (5.67–16.03) |
| Fixed-effects model | 100.0 | — | 11.26 (9.37–13.54) |
| Random-effects model | — | 100.0 | 11.26 (9.37–13.54) |




*Source:* Schumacher and colleagues (2014). Copyright © 2014, Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

*Note:* **CI =** confidence interval. "Panel A shows incidence-rate ratios for death from any cause, and Panel B shows incidence-rate ratios for death from lung cancer. The incidence rate is the number of events per 100 person-years. Person-years were attributed such that the incidence-rate ratios were equal to the reported mortality ratios implicitly, assuming that data were based on a homogeneous age group. Standard errors were not affected, since they depend only on the number of observed deaths. Since no study-specific detailed tables of data on persons who did not smoke were available, the group of nonsmokers in this forest plot is larger than the one used by Cochran and hence contains more observed deaths; to correct for this, standard errors were inflated accordingly. The horizontal lines represent confidence intervals, with arrows indicating extensions of the intervals. Boxes represent estimated incidence-rate ratios, with the sizes of the boxes indicating the inverse variance of the respective studies. Diamonds represent the pooled incidence-rate ratio. The width of the diamonds represents the width of the 95% confidence interval of the pooled incidence-rate ratio" (Schumacher et al. 2014, p. 187).

comparison revealed rising relative risks for all-cause mortality among current smokers, both men and women, in the contemporary cohorts. Among former smokers, the relative risks were substantially lower in the contemporary cohorts compared with those in the earlier American Cancer Society cohorts. However, compared with never smokers, the relative risks for former smokers were higher in the contemporary cohorts compared with the earlier cohorts (Tables 5.5a and 5.5b).

The 2014 Surgeon General's report also found that despite advancement in disease prevention and treatment over the past 50 years, current cigarette smokers had not experienced as much improvement in life expectancy compared with former and never smokers. Former smokers had progressively lower relative risk of all-cause mortality the younger they quit smoking (USDHHS 2014). For example, the Million Women Study found that women who quit smoking before 30 years of age and before 40 years of age avoided more than 97% and 90% of excess mortality risk, respectively, compared with those who continued smoking (Pirie et al. 2013). In an analysis of more than 216,000 adults from 1997 to 2004, Jha and colleagues (2013) found a similar relationship between smoking and survival: Smoking cessation before 40 years of age reduced the risk of death associated with continued smoking by approximately 90%. Additionally, adults who

**Table 5.5a Relative risks by smoking status and age group among adult men 35 years of age and older, United States**

| | Current smokers (years of age) | | | | Former smokers (years of age) | | | |
|---|---|---|---|---|---|---|---|---|
| | 35–54[a] | 55–64[b] | 65–74[b] | ≥75[b] | 35–54[a] | 55–64[b] | 65–74[b] | ≥75[b] |
| Lung cancer | 14.33 | 19.03 | 28.29 | 22.51 | 4.40 | 4.57 | 7.79 | 6.46 |
| Other cancers[c] | 1.74 | 1.86 | 2.35 | 2.18 | 1.36 | 1.31 | 1.49 | 1.46 |
| Coronary heart disease | 3.88 | 2.99 | 2.76 | 1.98 | 1.83 | 1.52 | 1.58 | 1.32 |
| Other heart disease[d] | — | — | 2.22 | 1.66 | — | — | 1.32 | 1.15 |
| Cerebrovascular disease | — | — | 2.17 | 1.48 | — | — | 1.23 | 1.12 |
| Other vascular diseases[e] | — | — | 7.25 | 4.93 | — | — | 2.20 | 1.72 |
| Diabetes mellitus | — | — | 1.50 | 1.00 | — | — | 1.53 | 1.06 |
| Other cardiovascular diseases[f] | 2.40 | 2.51 | — | — | 1.07 | 1.51 | — | — |
| Influenza, pneumonia, tuberculosis | — | — | 2.58 | 1.62 | — | — | 1.62 | 1.42 |
| Chronic obstructive pulmonary disease[g] | — | — | 29.69 | 23.01 | — | — | 8.13 | 6.55 |
| Influenza, pneumonia, tuberculosis, chronic obstructive pulmonary disease[h] | 4.47 | 15.17 | — | — | 2.22 | 3.98 | — | — |
| All causes | 2.55 | 2.97 | 3.02 | 2.40 | 1.33 | 1.47 | 1.57 | 1.41 |

*Source:* Analyses of Cancer Prevention Study II and updated analyses of the pooled contemporary cohort population described in Thun and colleagues (2013) provided to the Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.
[a]Relative risks for 35–54 years of age were obtained from Cancer Prevention Study.
[b]Relative risks for 55–64 years of age, 65–74 years of age, and 75 years of age and older were obtained from merged contemporary cohorts (Thun et al. 2013).
[c]Other cancers consist of cancers of the lip, pharynx and oral cavity, esophagus, stomach, pancreas, larynx, cervix uteri (women), kidney and renal pelvis, bladder, liver, colon and rectum, and acute myeloid leukemia.
[d]Other heart disease is composed of rheumatic heart disease, pulmonary heart disease, and other forms of heart disease.
[e]Other vascular diseases are composed of atherosclerosis, aortic aneurysm, and other arterial diseases.
[f]For 35–54 years of age and ages 55–64 years of age, other cardiovascular diseases are composed of other heart disease, cerebrovascular disease, other vascular diseases, and diabetes mellitus and were analyzed and reported as one category. A single relative risk based on combined conditions was used to compute smoking-attributable mortality. Relative risk based on combined conditions was used to compute smoking-attributable mortality in these age strata.
[g]Chronic obstructive pulmonary disease is composed of bronchitis, emphysema, and chronic airways obstruction.
[h]For 35–54 years of age and 55–64 years of age, influenza, pneumonia, tuberculosis, and chronic obstructive pulmonary disease were analyzed and reported as one category. A single relative risk based on combined conditions was used to compute smoking-attributable mortality.

**Table 5.5b Relative risks by smoking status and age group among adult women 35 years of age and older, United States**

| | Current smokers (years of age) | | | | Former smokers (years of age) | | | |
|---|---|---|---|---|---|---|---|---|
| | 35–54[a] | 55–64[b] | 65–74[b] | ≥75[b] | 35–54[a] | 55–64[b] | 65–74[b] | ≥75[b] |
| Lung cancer | 13.30 | 18.95 | 23.65 | 23.08 | 2.64 | 5.00 | 6.80 | 6.38 |
| Other cancers[c] | 1.28 | 2.08 | 2.06 | 1.93 | 1.24 | 1.28 | 1.26 | 1.27 |
| Coronary heart disease | 4.98 | 3.25 | 3.29 | 2.25 | 2.23 | 1.21 | 1.56 | 1.42 |
| Other heart disease[d] | — | — | 1.85 | 1.75 | — | — | 1.29 | 1.32 |
| Cerebrovascular disease | — | — | 2.27 | 1.70 | — | — | 1.24 | 1.10 |
| Other vascular diseases[e] | — | — | 6.81 | 5.77 | — | — | 2.26 | 2.02 |
| Diabetes mellitus | — | — | 1.54 | 1.10 | — | — | 1.29 | 1.06 |
| Other cardiovascular diseases[f] | 2.44 | 1.98 | — | — | 1.00 | 1.10 | — | — |
| Influenza, pneumonia, tuberculosis | — | — | 1.75 | 2.06 | — | — | 1.28 | 1.21 |
| Chronic obstructive pulmonary disease[g] | — | — | 38.89 | 20.96 | — | — | 15.72 | 7.06 |
| Influenza, pneumonia, tuberculosis, chronic obstructive pulmonary disease[h] | 6.43 | 9.00 | — | — | 1.85 | 4.84 | — | — |
| All causes | 1.79 | 2.63 | 2.87 | 2.47 | 1.22 | 1.34 | 1.53 | 1.43 |

*Source:* Analyses of Cancer Prevention Study II and updated analyses of the pooled contemporary cohort population described in Thun and colleagues (2013) provided to the Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.
[a]Relative risks for 35–54 years of age were obtained from Cancer Prevention Study.
[b]Relative risks for 55–64 years of age, 65–74 years of age, and 75 years of age and older were obtained from merged contemporary cohorts (Thun et al. 2013). Relative risks for other vascular diseases among women 55 years of age and older do not include data from the Women's Health Initiative of the National Heart, Lung, and Blood Institute.
[c]Other cancers consist of cancers of the lip, pharynx and oral cavity, esophagus, stomach, pancreas, larynx, cervix uteri (women), kidney and renal pelvis, bladder, liver, colon and rectum, and acute myeloid leukemia.
[d]Other heart disease is composed of rheumatic heart disease, pulmonary heart disease, and other forms of heart disease.
[e]Other vascular diseases are composed of atherosclerosis, aortic aneurysm, and other arterial diseases.
[f]For 35–54 years of age and ages 55–64 years of age, other cardiovascular diseases are composed of other heart disease, cerebrovascular disease, other vascular diseases, and diabetes mellitus and were analyzed and reported as one category. A single relative risk based on combined conditions was used to compute smoking-attributable mortality. Relative risk based on combined conditions was used to compute smoking-attributable mortality in these age strata.
[g]Chronic obstructive pulmonary disease is composed of bronchitis, emphysema, and chronic airways obstruction.
[h]For 35–54 years of age and 55–64 years of age, influenza, pneumonia, tuberculosis, and chronic obstructive pulmonary disease were analyzed and reported as one category. A single relative risk based on combined conditions was used to compute smoking-attributable mortality.

had quit smoking at 25–34, 35–44, or 45–54 years of age gained about 10, 9, and 6 years of life, respectively, compared with those who continued smoking. These findings are consistent with those reported in the 2004 and 2014 Surgeon General's reports. Although smokers lose an estimated decade of life on average, smoking cessation by 40 years of age avoided more than 90% of the excess mortality caused by continued smoking (USDHHS 2004, 2010; Pirie et al. 2013). Even quitting smoking by about 60 years of age could reduce premature mortality by 40% (USDHHS 2004, 2010).

## Summary of the Evidence

The health benefits of smoking cessation on all-cause mortality have been systematically reviewed in previous Surgeon General's reports (USDHHS 2004, 2014). The evidence published since the 1990 Surgeon General's report continues to affirm that smoking cessation at any age reduces the risk of premature death (Jha et al. 2013; Pirie et al. 2013; USDHHS 2014). The relative risk for dying from smoking has increased over time, but the benefit of quitting persists.

# Benefits of Smoking Cessation on Economic Costs

Cigarette smoking causes both substantial morbidity and premature mortality, resulting in significant economic costs for smokers and their families and very large costs for society in general (USDHHS 2004). Because smoking cessation reduces these costs, the comparative costs and benefits of treatments for smoking cessation will help to inform tobacco control strategies for different settings. In evaluating the economic dimensions of smoking cessation, consideration needs to be given to the specific costs and benefits generated by programs or policies that increase successful cessation. These costs and benefits, which extend into numerous sectors beyond healthcare, include the consequences for employment, such as lost productivity from active smoking, as well as for retirement benefits and pensions that may be transferred to never smokers and former smokers from early tobacco-related death among sustained smokers who do not quit (National Cancer Institute and World Health Organization 2016). This section focuses on the economic dimensions of smoking cessation, including the critical comparator: the costs of smoking.

## Economic Costs of Smoking

The economic costs of an intervention or managing a health outcome represent the opportunity cost of resources used, which includes direct costs, productivity losses, and intangible costs. Direct costs include direct medical and nonmedical costs; productivity losses—often referred as indirect costs—include the costs associated with morbidity and premature mortality; and intangible costs include such difficult-to-monetize consequences as pain and suffering and emotional well-being (Haddix et al. 2003). As with smoking-attributable increases in morbidity and premature mortality, the economic costs of smoking have been estimated for decades. Since 1991, for example, CDC has used the SAMMEC model to estimate the economic costs associated with lost productivity due to premature death from tobacco use (Shultz et al. 1991; USDHHS 2014). These estimates are produced by first estimating the total number of years of productive life lost from early mortality attributable to smoking and then converting that loss into financial terms to indicate monetary loss because of lost work productivity. Using the SAMMEC model, CDC estimated, for example, that the average annual smoking-attributable economic cost of lost productivity for 2000–2004 was $96.8 billion when premature mortality alone was considered (CDC 2008). Combining the costs of lost productivity with the direct healthcare expenditures attributable to smoking of $96 billion during the same period, the total annual smoking-attributable economic cost was $193 billion (CDC 2008). Using data linked between the 2006–2010 Medical Expenditure Panel Survey and the 2004–2009 National Health Interview Survey, the estimated annual healthcare expenditure attributable to smoking was as much as $170 billion in 2010 dollars; public programs—including Medicare, Medicaid, and other federally sponsored programs—accounted for more than 60% of this estimate (Xu et al. 2015b). However, these estimates underestimate the economic impact of smoking, because they do not account for smoking-related disability, smoking-related absenteeism from work, smoking-attributable loss of earnings, and morbidity and mortality attributable to exposure to secondhand smoke.

Regardless, national estimates that are similar to those presented above can be developed for states using the methodology underlying inclusive state-specific estimates, such as those for the state of California made by Max and colleagues (2016). The authors estimated smoking-attributable healthcare costs in California in 2009 using a series of econometric models, which estimated expenditures for such healthcare categories as hospital care, ambulatory care, prescriptions, and home health and nursing home care. An econometric model was also used to predict lost productivity because of illness, particularly how smoking status influenced the number of days absent from work. Premature mortality because of smoking was estimated using an epidemiologic approach. Using these approaches, Max and colleagues (2016) calculated $1.4 billion in lost productivity from illness and $6.8 million in lost productivity from premature mortality among smokers in California in 2009.

The 2014 Surgeon General's report used three different approaches, all based on the SAMMEC methodology, to derive updated estimates of smoking-attributable direct healthcare expenditures (USDHHS 2014):

1. Using medical service costs from 2009, the estimated aggregated annual healthcare expenditure attributable to cigarette smoking was $132.5 billion in 2009 dollars. Using the Medical Care part of the Consumer Price Index to account for inflation (available from the U.S. Bureau of Labor Statistics [2017]), the expenditure in 2017 dollars was $167.7 billion.

2. Using age- and sex-specific relative risks, the estimated smoking-attributable direct healthcare spending was

$175.9 billion (in 2013 dollars) and $196.7 billion in 2017 dollars.

3. Using a two-part regression analysis of Medical Expenditure Panel Survey (MEPS) data, the estimated smoking-attributable direct healthcare spending was $169.3 billion (in 2010 dollars) and $207.2 in 2017 dollars (Xu et al. 2015b).

4. The 2014 Surgeon General's report also used updated lifetables and estimates of the present value of future earnings to estimate the smoking-attributable economic cost of lost productivity; the estimate was $150.7 billion in 2009 dollars ($190.7 billion in 2017 dollars) (USDHHS 2014). Moreover, the report estimated the economic cost of lost productivity because of exposure to secondhand smoke to be an additional $5.7 billion in 2009 dollars ($7.2 billion in 2017 dollars), a figure that did not account for direct healthcare expenditures attributable to exposure to secondhand smoke (USDHHS 2014). The value of lost productivity attributable to premature death from smoking was $172.2 billion in 2009 ($217.9 billion in 2017 dollars), and the cost attributable to exposure to secondhand smoke was $6.5 billion in 2009 ($8.2 billion in 2017 dollars).

On the basis of these updated estimates, the 2014 Surgeon General's report concluded that the costs of cigarette smoking represented a significant portion (7.6–8.7%) of healthcare expenditures in the United States (USDHHS 2014).

The SAMMEC model uses a cross-sectional approach to determine the economic expenditures of smoking; it estimates the burden of smoking-related disease and death of smokers compared with having a population of all nonsmokers and calculates the disease-attributable smoking expenditures within a specific period. Another method for evaluating the overall economic costs of smoking is the life-cycle approach, which estimates the present value of the cost of adding a smoker to society and also considers that benefits from longer lives because of smoking cessation or prevention will be mitigated because of other costs later in life. The life-cycle approach has been implemented using various datasets from national panels in the United States.

Sloan and colleagues (2004) used a life-cycle approach to estimate the overall cost of smoking. They incorporated private costs to smokers, including disability and absenteeism; external costs to society, including Social Security benefits, pensions, and life insurance; and quasi-external costs to family members because of their exposure to secondhand smoke. The authors estimated that each new cohort of U.S. smokers, beginning at 24 years of age, added $203.8 billion of new lifetime costs (in year 2000 dollars). Most of the lifetime costs to society were private ($168.5 billion), but external and quasi-external costs (costs imposed by smoking on the spouse and children of a smoker) (total of $35.3 billion) were substantial, even after accounting for federal and state tobacco excise taxes at the time of estimation. These external and quasi-external costs are much higher than previous estimates of externalities from cigarette smoking, primarily because of a better understanding of health effects from exposure to secondhand smoke (Chaloupka and Warner 2000; Sloan et al. 2004). Although these estimates suggest that a rational decision maker would never choose to initiate tobacco use, individual decision making may highly discount future negative events for perceived current effects and may be further affected by the limited information on risk considered by potential smokers (Gruber and Koszegi 2001; Gruber 2002).

Regardless of underlying methodology, these estimates document the substantial costs associated with smoking. However, these macro-level costs hide the significant costs incurred by the households of smokers, which include not only the costs of purchasing tobacco products but also economic losses because of absenteeism from work—because of smoking-related morbidity—and of the direct costs of healthcare. Such household costs are differentially distributed in the United States, given the strong gradient of less smoking with increasing income (CDC 2011). Furthermore, the estimated total costs include only direct costs and productivity losses; these estimates do not consider harder-to-quantify and intangible costs, such as those from the grief and suffering of family members and friends of ill smokers. Those costs can be measured through surveys using a "willingness-to-pay" approach, which asks how much a person would pay to avoid such a scenario. Costs estimated through willingness-to-pay approaches are often much larger than costs that are measured directly (Gold et al. 1996).

## Economics of Smoking Cessation

An economic analysis of smoking cessation must consider a variety of costs, including costs accrued by smokers before successful cessation. Although many persons can quit smoking without any assistance, others need assistance from public health programs that encourage smoking cessation, or from healthcare services that provide psychological or pharmacologic assistance to help them stop smoking. These interventions, which increase smoking cessation, also have associated costs.

### Principles of Cost-Benefit and Cost-Effectiveness Analysis

Policies to encourage beneficial behaviors are often evaluated by cost-benefit analysis, which compares outcomes in terms of dollar value and prioritizes different policies, particularly when resources are scarce or funds are limited (Russell 2015). The simplest method for comparison is to derive a single estimate for each policy by converting all costs and benefits into financial measures. In healthcare, however, the full benefits associated with improved health are not easily converted into financial benefits because of challenges in the financial valuations of extending life or avoiding morbidity (Gold et al. 1996). As a result, cost-effectiveness analysis is often used in healthcare, but the measurements of effect may not always be comparable across studies. One type of cost-effectiveness analysis is cost-utility analysis, in which health benefits are based on a common metric, such as quality-adjusted life-years (QALYs) gained (Gold et al. 1996). Recommendations on cost-effectiveness in health and medicine were published in 1996 (Gold et al. 1996; Russell et al. 1996; Siegel et al. 1996; Weinstein et al. 1996) and updated in 2016 (Sanders et al. 2016).

The particular analytic perspective to choose and the evaluation of ratios are two key considerations for both cost-benefit and cost-effectiveness analyses. The analytic perspective taken can change the costs and benefits of an evaluation, because evaluations using one perspective (e.g., that of a payer) may not include the same costs or benefits as those using another perspective (e.g., that of society in general). For example, if an insurance plan accrues the costs of paying for a smoking cessation program but does not reap the benefits from cessation because persons frequently switch insurance plans, such switching may result in a less cost-effective scenario for the plan. From a societal perspective, however, benefits are accrued from all persons who quit successfully, regardless of switches in insurance plans. Gold and colleagues (1996) recommended the societal perspective as the appropriate analytic perspective to provide a full accounting of costs and benefits, but other perspectives, such as that of the payer when a program to promote smoking cessation is implemented, may be the focus of an analysis. Sanders and colleagues (2016) recommended considering components of cost from an analytical perspective (e.g., from health sector and societal perspectives).

To assess the cost-effectiveness of an intervention, the incremental cost-effectiveness ratio is calculated and evaluated. The ratio estimates how much extra cost is needed for an intervention compared with alternatives (control or next best alternative in terms of effectiveness) to derive an extra unit of benefit (e.g., QALY). To compare the relative value of multiple policy interventions, both absolute cost-effectiveness ratio (the ratio of the cost of intervention minus costs averted by the intervention, divided by QALYs gained, where the comparison is between an intervention and a "do nothing" or control) and incremental cost-effectiveness ratio (the ratio of costs of interventions minus costs averted by the intervention, divided by QALYs gained, where the comparison is between an intervention and the next best intervention) can be estimated (Cohen and Reynolds 2008). When evaluating one intervention versus a control, the absolute cost-effectiveness and incremental cost-effectiveness are the same. However, an evaluation of multiple interventions should be based on incremental cost-effectiveness ratios. Relying only on absolute cost-effectiveness ratios can distort estimates and result in invalid conclusions. The absolute cost-effectiveness ratios of alternative interventions can be similar and cost-effective when compared with an acceptable threshold. However, when the incremental cost-effectiveness ratio for an alternative is evaluated and compared with the next best alternative, the alternative may not necessarily be cost-effective—even if it is cost-effective when compared with the control.

An international consortium that evaluated the relative costs and benefits of a range of smoking cessation interventions found that in a high-income country, such as the United States, such interventions as automated text messaging, self-help materials, and brief advice from a physician have a low cost but only small effects on smoking cessation. Conversely, pharmacological and psychological interventions (either by telephone or provided in person) are higher in cost but have greater effects on increasing smoking cessation (West et al. 2015). In another examination of relative costs and benefits that used a much different framework to gauge benefit, disability-adjusted life-years gained, Jha and colleagues (2006) found that NRT may be more cost-effective than other interventions—its higher price notwithstanding. A systematic review on the economic impact of a conservative 20% price increase of tobacco products through taxation found evidence of per capita cost savings over the short- and medium terms (Contreary et al. 2015).

Because of their relatively high cost, pharmacologic and psychologic smoking cessation interventions have been more closely evaluated than inexpensive interventions. This report summarizes the cost-effectiveness ratios gleaned from the review of literature on the cost-effectiveness of clinical cessation interventions and compares the estimates to a threshold of cost-effectiveness for clinical interventions used in healthcare (Neumann et al. 2014; Sanders et al. 2016).

### Cost-Effectiveness of Clinical Smoking Cessation Interventions

In a systematic review of the literature, Ruger and Lazar (2012) summarized the evidence on the cost-effectiveness of smoking cessation through 2009. This review covered literature indexed in PubMed and the British National Health Service's Economic Evaluation Database as containing an economic evaluation (cost-benefit, cost-effectiveness, cost-utility, or cost-minimization analysis) of pharmacotherapy or counseling for smoking cessation. The review examined 36 economic evaluations in detail, including 14 studies of NRT, 12 studies of non-nicotine-based pharmacotherapy, and 10 studies of brief counseling for smoking cessation. The review found that cost-effectiveness and other types of economic evaluation studies do not routinely use standard metrics to evaluate benefits and often use the payer's perspective, not the societal perspective as recommended (Tables 5.6–5.8). To standardize dollar value of costs to the same base year, estimates in this section were converted to 2017 U.S. dollars from the base case year (or publication year if the base case year was not known) using the Medical Care part of the Consumer Price Index (all urban consumers). When performing benefit-cost analyses, USDHHS typically values QALY gains at about $500,000 or $850,000, depending on the discount rate applied (USDHHS 2016). This is substantially larger than the recently recommended values of $100,000 or $150,000 per QALY gained (Neumann et al. 2014).

Table 5.6 summarizes studies on nicotine-based pharmacotherapies. For NRT, RCTs in the United Kingdom estimated that when NRT was added to brief counseling in primary care settings, incremental cost per life-year saved ranged from $1,115 to $2,541 depending on the age groups from the national health system perspective (Stapleton et al. 1999). According to two more recent studies, the cost of NRT per additional quitter was $171 compared with usual care from the health insurance perspective (Salize et al. 2009) and was $3,781 compared with brief counseling from the state program perspective (Hollis et al. 2007). In an examination of observational data, adding free NRT to quitline counseling in the United States resulted in incremental costs of $132 per life-year saved and $267 per quit attempt in Oregon from the program perspective (Fellows et al. 2007) and of $808 per quit attempt in Minnesota from the funding agency perspective (An et al. 2006). Three studies that used decision-analytic modeling found incremental cost-effectiveness ratios ranging from $9,463 to $23,589 per QALY gained for physician-based cessation counseling with nicotine patch compared with counseling alone from the payer perspective (Fiscella and Franks 1996), $2,388 to $9,791 per QALY gained from the societal perspective (Cromwell et al. 1997), and $2,511 to $6,020 per life-year saved for NRT compared with counseling or advice alone from the national health services perspective (Song et al. 2002).

Five studies that modeled populations of smokers estimated incremental cost-effectiveness ratios for counseling and NRT compared with brief physician counseling alone ranged from $1,267 to $42,160 per life-year saved from the payer perspective (Oster et al. 1986; Wasley et al. 1997; Gilbert et al. 2004; Cornuz et al. 2006) and from $2,021 to $9,002 per QALY gained from the societal perspective (Feenstra et al. 2005). Among two studies on pharmacist-directed smoking cessation programs, one involving only the receipt of advice and motivation compared with usual advice from a pharmacist found cost-effectiveness ratios ranging from $628 to $2,678 per life-year saved from the payer perspective (Crealey et al. 1998), and the other incorporating four methods under pharmacist direction (quitting cold turkey, two kinds of NRT, and bupropion) compared with self-directed quit attempts found cost-effectiveness ratios ranging from $478 to $2,496 per successful quit from the payer perspective (Tran et al. 2002).

Table 5.7 summarizes cost-effectiveness studies of non-nicotine-based pharmacotherapies. Five studies evaluated varenicline and compared it with different comparators (nortryptiline; bupropion, NRT, and unaided cessation; brief counseling alone and unaided cessation; counseling; or NRT). Incremental cost-effectiveness ratios ranged from $1,409 to $5,838 per quit attempt from the healthcare system perspective (Hoogendoorn et al. 2008) and from dominates (i.e., less costly and more effective) to $4,981 per QALY gained from the healthcare payer/system perspective (Hoogendoorn et al. 2008; Howard et al. 2008; Annemans et al. 2009; Bolin et al. 2009b; Igarashi et al. 2009). In some trials, varenicline was more efficacious than the comparison strategy (whether unaided cessation or cessation with NRT or bupropion) and more cost-effective from various perspectives (healthcare payer/system) (Howard et al. 2008; Annemans et al. 2009; Bolin et al. 2009b; Igarashi et al. 2009). Two other studies also showed that an extended period of varenicline treatment compared with placebo or 12 weeks of varenicline, bupropion, or NRT was less costly and more effective per QALY gained from the healthcare perspective (Knight et al. 2010) and was more effective than placebo, with incremental cost-effectiveness ratios as high as $41,053 per QALY gained from the societal perspective (Bolin et al. 2009a). Studies comparing bupropion with NRT found incremental cost-effectiveness ratios as high as $1,223 per QALY gained from the societal perspective (Bolin et al. 2006). One study compared bupropion with counseling or advice alone and found that the incremental cost per life-year saved ranged from $1,603 to $3,746 from a national health system perspective (Song et al. 2002).

Table 5.8 summarizes 10 studies that evaluated brief counseling therapies conducted with a variety of methods, in diverse settings, and with diverse populations. Using data from RCTs, an evaluation of care that included 20 minutes of bedside counseling, 12 minutes of videos, self-help materials, and follow-up calls found

**Table 5.6 Summary of economic evaluations of nicotine-based pharmacotherapies for smoking cessation**

| Study | Design/population | Effects | Costs | Outcomes/findings |
|---|---|---|---|---|
| Oster et al. (1986) | • Meta-analysis<br>• Cost-effectiveness analysis<br>• Hypothetical group of smokers seen in routine office visits<br>• Intervention/comparison:<br>– Physician advice and counseling alone<br>– Nicotine gum and physician advice<br>• Perspective: Payer<br>• Lifetime | • Life-years saved | • Physician time and gum<br>• Base year: 1984<br>• Source: Retail prices, salary rates | • Range of cost per life-year saved, by sex:<br>• Men: $4,113–$6,465 ($18,305–$28,773 in 2017 $)<br>• Women: $6,880–$9,473 ($30,620–$42,160 in 2017 $) |
| Fiscella and Franks (1996) | • Decision analytic model<br>• Cost-effectiveness and cost-utility analyses<br>• Male and female smokers, 25–69 years of age receiving primary care<br>• Intervention/comparison:<br>– Physician-based smoking cessation counseling with nicotine patch<br>– Physician-based smoking cessation counseling alone<br>• Perspective: Payer<br>• Lifetime | • QALYs saved | • Physician time and retail price of nicotine patch<br>• Base year: 1995<br>• Source: Published average wholesale price | • The nicotine patch produced one additional lifetime quitter at a cost of $7,332 ($15,805 in 2017 $)<br>• Range of incremental cost-effectiveness of the nicotine patch, by sex:<br>• Men: $4,390–$10,943 per QALY ($9,463–$23,589 per QALY in 2017 $)<br>• Women: $4,955–$6,983 per QALY ($10,681–$15,053 per QALY in 2017 $) |
| Cromwell et al. (1997) | • Decision probabilities model<br>• Cost-effectiveness analysis of clinical practice guidelines and cost-utility analysis<br>• Simulated model of U.S. smokers, 18 years of age or older who were willing to make a quit attempt within 1 year<br>• Intervention/comparison: Model of five counseling interventions for primary care physicians (minimal, brief, and full) and specialists (individual intensive and group intensive) with and without transdermal nicotine and nicotine gum<br>• Perspective: Societal<br>• 1 year | • QALYs and life-years saved<br>• Quit rates | • Implementation of guidelines (screening, advice, motivational sessions, and interventions)<br>• Base year: 1995<br>• Source: Published literature, guideline reports, and Medicare charges | • Implementing the guidelines cost $3,779 ($8,146 in 2017 $) per quitter, $2,587 ($5,577 in 2017 $) per life-year saved, and $1,915 ($4,128 in 2017 $) per QALY saved<br>• Costs per QALY ranged from $1,108 to $4,542 ($2,388 to $9,791 in 2017 $)<br>• More intensive interventions were more cost-effective than those with less intensity |

**Table 5.6 Continued**

| Study | Design/population | Effects | Costs | Outcomes/findings |
|---|---|---|---|---|
| Wasley et al. (1997) | • Meta-analysis<br>• Cost-effectiveness analysis<br>• Hypothetical samples of 400 smokers who smoke ≥20 cigarettes per day<br>• Intervention/comparison:<br>• Nicotine patch with brief counseling<br>• Brief physician counseling alone<br>• Perspective: Payer<br>• Lifetime | • Life-years saved<br>• Quit rates | • Physician time and nicotine patch<br>• Base year: 1995<br>• Source: Average retail cost and physicians' medical fee schedules | • Range of average cost per life-year saved, by sex:<br>• Men: $965–$1,585 ($2,080–$3,417 in 2017 $)<br>• Women: $1,634–$2,360 ($3,522–$5,087 in 2017 $)<br>• Range of incremental cost per life-year saved, by sex:<br>• Men: $1,796–$2,949 ($3,872–$6,357 in 2017 $)<br>• Women: $3,040–$4,391 ($5,553–$9,379 in 2017 $) |
| Crealey et al. (1998) | • Case control<br>• Cost-effectiveness analysis<br>• Matched cases (52) and controls (60) in PAS model program in Northern Ireland<br>• Intervention/comparison:<br>• Cases received advice and motivation to quit from pharmacist<br>• Matched controls received usual advice from pharmacists<br>• Perspective: Payer<br>• Lifetime | • Life-years saved | • Direct intervention (PAS materials, training for pharmacists, and time spent counseling)<br>• Base year: 1997<br>• Source: Estimates of program costs and salary rates | • Range of cost for PAS program per life-year saved, by sex:<br>• Men: $337–$603 ($683–$1,222 in 2017 $)<br>• Women: $310–$1,322 ($628–$2,678 in 2017 $) |
| Stapleton et al. (1999) | • Randomized controlled trial and survey<br>• Cost-effectiveness analysis<br>• 1,200 patients who smoked ≥15 cigarettes per day in 15 English counties<br>• Intervention/comparison:<br>• Brief counseling with general practitioner plus 16-hour nicotine patch treatment and booklet<br>• Brief counseling with general practitioner survey plus placebo and booklet<br>• Perspective: National Health Service<br>• 12 weeks | • Life-years saved | • Treatment (counseling time, nicotine patches, patient booklets, and biochemical validation of abstinence)<br>• Base year: 1998<br>• Source: National survey data and resource use | • Incremental cost per life-year saved among patients if practitioners could prescribe nicotine patch, by age group:<br>• <35 years: $656 ($1,288 in 2017 $)<br>• 35–44 years: $568 ($1,115 in 2017 $)<br>•<br>• 55–65 years: $1,294 ($2,541 in 2017 $) |

**Table 5.6 Continued**

| Study | Design/population | Effects | Costs | Outcomes/findings |
|---|---|---|---|---|
| Tran et al. (2002) | • Observations<br>• Cost-effectiveness and cost-utility analyses<br>• 48 patients 21–70 years of age who had tried at least once to quit smoking<br>• Intervention/comparison:<br>• Pharmacist-directed smoking cessation program using four methods (cold turkey, nicotine patch, nicotine gum, bupropion)<br>• Self-directed quit attempt<br>• Perspective: Payer and societal<br>• 1 year, lifetime | • Quit rate<br>• Life-years saved<br>• QALYs saved | • Materials and pharmacist time<br>• Selected cessation methods (retail cost)<br>• Base year: 1997<br>• Source: Salary data and retail costs | • Incremental costs (in 2017 $) using pharmacist-directed program, by method of smoking cessation per successful quit from the payer perspective:<br>– $236 ($478 in 2017 $) for cold turkey<br>– $936 ($1,896 in 2017 $) for nicotine patch<br>– $1,232 ($2,496 in 2017 $) for nicotine gum<br>– $1,150 ($2,370 in 2017 $) for bupropion |
| Gilbert et al. (2004) | • Markov chain cohort simulation<br>• Cost-effectiveness analysis<br>• Two simulated cohorts of smokers in Seychelles (Africa)<br>• Intervention/comparison:<br>• Physician counseling alone<br>• Counseling plus one of five cessation therapies (nicotine gum, patch, spray, inhaler, or bupropion)<br>• Perspective: Third-party payer<br>• Lifetime | • Life-years saved | • Additional physician time required<br>• Treatment (retail prices for generic treatment medications)<br>• Base year: 2002–2003<br>• Source: Retail prices and wage data | • Incremental cost per life-year saved, by type of therapy (U.S. prices):<br>– $3,712 ($5,939 in 2017 $) for nicotine gum<br>– $1,982 ($3,171 in 2017 $) for nicotine patch<br>– $4,597 ($7,355 in 2017 $) for nicotine spray<br>– $4,291 ($6,865 in 2017 $) for nicotine inhaler<br>– $1,324 ($2,118 in 2017 $) for bupropion |
| Feenstra et al. (2005) | • RIVM chronic disease<br>• Cost-effectiveness and cost-utility analyses<br>• Smokers in the Netherlands<br>• Intervention/comparison:<br>– Minimal counseling by a general practitioner with or without NRT<br>– Intensive counseling by a general practitioner with NRT or bupropion<br>– Telephone counseling<br>• Perspective: Societal<br>• 1, 10, or 75 years | • Quit rate<br>• Life-years gained<br>• QALYs gained | • Intervention<br>• Healthcare for 11 smoking-related diseases (direct costs only)<br>• Base year: 2000<br>• Source: Estimated retail costs, standard costing manual, and salary data | • Cost per QALY gained ranged from $1,109 ($2,021 in 2017 $) for telephone counseling to $4,939 ($9,002 in 2017 $) for intensive counseling with nicotine patches or gum |

**Table 5.6 Continued**

| Study | Design/population | Effects | Costs | Outcomes/findings |
|---|---|---|---|---|
| An et al. (2006) | • Before and after initiative<br>• Cost-effectiveness analysis<br>• 373 callers to the Minnesota QUITPLAN helpline<br>• Intervention/comparison:<br>– Quitline callers before initiative<br>– Quitline callers enrolled in multisession counseling received NRT (patch or gum) by mail<br>• Perspective: Funding agency<br>• 6 months | • Quit rate | • Counseling and provision of free NRT<br>• Base year: Not available<br>• Source: Estimated program costs | • Average number of ex-smokers per month increased from 16 to 124<br>• Average cost per quit increased from $1,362 ($1,926 in 2017 $) to $1,934 ($2,734 in 2017 $) |
| Cornuz et al. (2006) | • Markov-chain cohort simulation<br>• Cost-effectiveness analysis<br>• Simulated cohorts of smokers in six countries (Canada, France, Spain, Switzerland, United States, and United Kingdom)<br>• Intervention/comparison:<br>– Brief cessation counseling by general practitioner<br>– Counseling plus NRT<br>• Perspective: Third-party payer<br>• Lifetime | • Life-years saved | • Additional physician time required plus medications (retail price)<br>• Base year: 2002–2003<br>• Source: Pharmacy prices and published price data from each country | • Range of cost per life-year saved, by type of therapy and sex:<br>– Gum:<br>○ $2,230 for men ($3,568 in 2017 $)<br>○ $7,643 for women ($12,228 in 2017 $)<br>– Patch:<br>○ $1,758 for men ($2,813 in 2017 $)<br>○ $5,131 for women ($8,209 in 2017 $)<br>– Spray:<br>○ $1,935 for men ($3,096 in 2017 $)<br>○ $7,969 for women ($12,749 in 2017 $)<br>– Inhaler:<br>○ $3,480 for men ($5,568 in 2017 $)<br>○ $8,700 for women ($13,919 in 2017 $)<br>– Bupropion:<br>○ $792 for men ($1,267 in 2017 $)<br>○ $2,922 for women ($4,675 in 2017 $) |
| Fellows et al. (2007) | • Before and after free-patch initiative<br>• Cost-effectiveness analysis<br>• 959 smokers who registered for quitline service in Oregon<br>• Intervention/comparison:<br>– Pre-initiative program<br>– Free-patch initiative from the Oregon tobacco quitline<br>• Perspective: Program<br>• 1 year | • Quit rate<br>• Life-years saved | • Media and intervention (before and after the initiative)<br>• Base year: 2004<br>• Source: Quitline utilization and cost data from state, intervention providers, and patients | • Compared with the program before the free-patch initiative, the new initiative increased quitting fourfold and reduced total costs per quit by $2,688 ($4,120 in 2017 $)<br>• Free-patch initiative cost $86 ($22–$353) ($132 [$34–$541] in 2017 $) per life-year saved and $174 ($267 in 2017 $) per additional quit attempt |

**Table 5.6 Continued**

| Study | Design/population | Effects | Costs | Outcomes/findings |
|---|---|---|---|---|
| Hollis et al. (2007) | • Randomized trial<br>• Cost-effectiveness analysis<br>• 4,614 callers to the Oregon tobacco quitline who smoked ≥5 cigarettes per day<br>• Intervention/comparison: Brief, moderate, and intensive telephone counseling with or without offers of free nicotine patches<br>• Perspective: State program<br>• 1 year | • Abstinence rate | • Interventions<br>• Base year: 2004<br>• Source: Program records of resources consumed | • Compared with brief counseling with no NRT, the added costs for each additional quit were:<br>– $2,467 ($3,781 in 2017 $) for brief counseling plus NRT<br>– $1,912 ($2,931 in 2017 $) for moderate counseling and no NRT<br>– $2,109 ($3,233 in 2017 $) for moderate counseling plus NRT<br>– $2,640 ($4,047 in 2017 $) for intensive counseling and no NRT<br>– $2,112 ($3,237 in 2017 $) for intensive counseling plus NRT |
| Salize et al. (2009) | • Cluster randomized trial<br>• Cost-effectiveness analysis<br>• 577 patients who smoked ≥10 cigarettes per day in Germany<br>• Intervention/comparison:<br>– Training of general practitioners plus remuneration for each abstinent patient<br>– Training of general practitioners plus cost-free NRT and/or bupropion hydrochloride<br>– A combination of both strategies<br>• Perspective: Health insurance<br>• 1 year | • Abstinence rate | • Interventions<br>• Base year: 2003<br>• Source: Unit costs per each element of treatment in the trial | • Compared with usual care, both training of general practitioners plus drugs and training of general practitioners plus drugs and remuneration were cost-effective<br>• The cost per additional quitter was $107 ($171 in 2017 $) per patient for training of general practitioners plus drugs and $97 ($155 in 2017 $) per patient for training of general practitioners plus drugs and remuneration |

*Source:* Table 4 in Ruger and Lazar (2012).

*Notes:* **NRT =** nicotine replacement therapy; **PAS =** pharmacists action on smoking; **QALYs =** quality-adjusted life-years; **RIVM =** chronic disease model developed at the National Institute of Public Health and the Environment in The Netherlands. Estimates converted to 2017 U.S. dollars from the base case year (or publication year if no base case year) using the Medical Care part of the Consumer Price Index (all urban consumers).

**Table 5.7 Summary of economic evaluations of non-nicotine-based pharmacotherapies for smoking cessation**

| Study | Design/population | Effects | Costs | Outcomes/findings |
|---|---|---|---|---|
| Song et al. (2002) | • Decision analytic model<br>• Cost-effectiveness analysis<br>• Simulation based on results from published studies<br>• Intervention/comparison:<br>– Advice or counseling alone<br>– Advice or counseling plus NRT or bupropion sustained release<br>– Advice or counseling plus NRT and bupropion sustained release<br>• Perspective: United Kingdom National Health Services<br>• 1 year | • Quit rates<br>• Life-years saved | • Intervention<br>• Base year: 2001<br>• Source: Published studies | • Range of incremental cost per life-year saved compared with counseling or advice alone, by type of intervention:<br>– $1,441–$3,455 ($2,511–$6,020 in 2017 $) for NRT<br>– $920–$2,150 ($1,603–$3,746 in 2017 $) for bupropion sustained release<br>– $1,282–$2,836 ($2,234–$4,941 in 2017 $) for NRT plus bupropion sustained release |
| Antoñanzas and Portillo (2003) | • Adaptation of health and economic consequences of smoking interactive simulation<br>• Cost-effectiveness analysis<br>• Smokers in Spain<br>• Intervention/comparison:<br>– Bupropion<br>– NRT (nicotine patch or gum)<br>• Perspective: National health system<br>• 20 years | • Deaths prevented<br>• Life-years saved | • Intervention<br>• Healthcare costs for tobacco-related diseases or conditions (cancers, CHD, stroke, COPD, and low birth weight)<br>• Base year: 1999<br>• Source: National Health Survey and National Institute of Statistics | • At 20 years, for bupropion and the nicotine patch, respectively, there was a net savings of $32,920 ($62,441 in 2017 $) and $15,993 ($30,334 in 2017 $) per death prevented and a net savings of $3,852 ($7,306 in 2017 $) and $1,867 ($3,541 in 2017 $) per life-year saved<br>• At 20 years, nicotine gum had a cost-effectiveness ratio of $41,325 ($78,402 in 2017 $) per death prevented and $4,786 ($9,078 in 2017 $) per life-year saved |
| Bolin et al. (2006) | • Global health outcomes simulation model<br>• Cost-effectiveness analysis<br>• Model cohort of male and female smokers in Sweden<br>• Intervention/comparison:<br>– Bupropion<br>– NRT (nicotine patches and gum)<br>• Perspective: Societal<br>• 20 years | • QALYs gained | • Intervention<br>• Direct costs of smoking (COPD, asthma, CHD, stroke, and lung cancer)<br>• Reduced production and consumption (indirect costs of smoking)<br>• Base year: 2001<br>• Source: Swedish unit costs, hospital records, and physician records | • When direct and indirect costs on production and consumption were included, bupropion was cost-saving compared with both types of NRT<br>• When only direct costs were included, incremental cost per QALY gained for bupropion compared with nicotine patches was $702 ($1,223 in 2017 $) for men and $521 ($908 in 2017 $) for women |

**Table 5.7 Continued**

| Study | Design/population | Effects | Costs | Outcomes/findings |
|---|---|---|---|---|
| Halpern et al. (2007) | • Decision analytic model<br>• Cost-effectiveness analysis<br>• Simulation in cohort of 1,000 smokers in the United States<br>• Intervention/comparison:<br>– Varenicline (12 weeks)<br>– Nicotine patch (9 weeks)<br>– Bupropion (12 weeks)<br>– No intervention<br>• Perspective: Private health plans, state Medicaid program, and employer 10 years | • Abstinence rates | • Intervention<br>• Medical care for smoking-related diseases (CHD, COPD, and lung cancer) and pregnancy complications<br>• Productivity losses and absenteeism<br>• Base year: 2005<br>• Source: Literature | • Compared with unaided cessation, cost-effectiveness of varenicline per additional cessation at 2 years ranged from $648 ($953 in 2017 $) in the private health plan model to $1,229 ($1,049 in 2017 $) in the Medicaid model |
| Hoogendoorn et al. (2008) | • BENESCO model<br>• Cost-effectiveness and cost-utility analyses<br>• Hypothetical cohort of Dutch smokers making a one-time quit attempt<br>• Intervention/comparison:<br>– Varenicline<br>– Untreated or treated with bupropion, nortriptyline, or NRT<br>• Perspective: Dutch healthcare system<br>• Lifetime | • Quit rate<br>• QALYs gained | • Intervention<br>• Direct medical costs of smoking-related diseases (COPD, lung cancer, CHD, and stroke)<br>• Base year: 2004<br>• Source: Estimates from Dutch source data | • Varenicline estimated to cost $1,472 ($2,256 in 2017 $) per QALY gained compared with nortriptyline and $285 ($437 in 2017 $) per QALY gained compared with unaided cessation<br>• Cost of varenicline per additional quitter ranged from $919 ($1,409 in 2017 $) compared with NRT to $3,809 ($5,838 in 2017 $) compared with nortriptyline |
| Jackson et al. (2007) | • Decision tree model<br>• Cost-benefit analysis<br>• Simulation based on published results of clinical trial<br>• Intervention/comparison:<br>– Varenicline<br>– Bupropion (brand and generic)<br>– Placebo<br>• Perspective: Employer<br>• 1 year | • Quit rates | • Intervention<br>• Cost of smoking for employer (absenteeism, medical care, time lost, and insurance)<br>• Base year: 2006<br>• Source: Study detailing direct and indirect costs of smoker to an employer, and pricing related to wholesale acquisition costs | • Cost savings per nonsmoking employee at 1 year, by type of intervention:<br>– $541 ($765 in 2017 $) for varenicline<br>– $270 ($382 in 2017 $) for bupropion sustained release (generic)<br>– $151 ($213 in 2017 $) for bupropion sustained release (brand)<br>– $82 ($116 in 2017 $) for placebo |

**Table 5.7 Continued**

| Study | Design/population | Effects | Costs | Outcomes/findings |
|---|---|---|---|---|
| Howard et al. (2008) | • BENESCO Markov simulation<br>• Cost-utility analysis<br>• Hypothetical cohort of U.S. adult smokers who make a one-time quit attempt<br>– Intervention/comparison:<br>– Varenicline<br>– Bupropion<br>– NRT<br>– Unaided quitting<br>• Perspective: U.S. healthcare system<br>• 20 years and lifetime | • QALYs | • Intervention<br>• Direct lifetime costs of smoking-related diseases (lung cancer, COPD, CHD, stroke, and asthma)<br>• Base year: 2005 | • Varenicline was less costly and more effective (dominates) than other cessation strategies (bupropion, NRT, and unaided cessation) over either time period studied (20 years and lifetime) |
| Annemans et al. (2009) | • BENESCO Markov simulation<br>• Cost-effectiveness and cost-utility analyses<br>• Cohort of Belgian adult smokers making a one-time quit attempt<br>• Intervention/comparison:<br>– Varenicline, bupropion, or NRT with brief counseling<br>– Brief counseling alone<br>– Unaided cessation<br>• Perspective: Healthcare payer (public<br>• and private)<br>• Lifetime | • Life-years gained<br>• QALYs gained | • Intervention<br>• Direct medical costs related to smoking comorbidities (COPD, lung cancer, CHD, stroke, and asthma)<br>• Base year: 2007<br>• Source: Literature and public health databases | • Compared with brief counseling alone and unaided cessation, varenicline cost $337 ($456 in 2017 $) per life-year gained and $2,325 ($3,148 in 2017 $) per QALY gained<br>• Varenicline is cost-saving compared with bupropion and NRT |
| Bolin et al. (2009a) | • BENESCO Markov simulation<br>• Cost-utility analysis<br>• Simulated cohort of adult smokers in Sweden who successfully abstained after an initial<br>• 12-week treatment of varenicline<br>• Intervention/comparison:<br>– Additional 12 weeks of varenicline<br>– Placebo<br>• Perspective: Societal<br>• 50 years | • QALYs gained | • Intervention<br>• Average direct medical costs from smoking-related diseases (COPD, CHD, stroke, and lung cancer)<br>• Average value of indirect effects (reduced consumption and production)<br>• Base year: 2003<br>• Source: Healthcare cost data from Skåne, Sweden; estimated prescription prices; and published literature | • Incremental costs per QALY for additional 12 weeks of varenicline compared with placebo were $7,420 ($11,871 in 2017 $) for men and $7,464 ($11,941 in 2017 $) for women<br>• Incremental costs per QALY, including indirect effects, were $25,359 ($40,571 in 2017 $) for men and $25,660 ($41,053 in 2017 $) for women |

**Table 5.7 Continued**

| Study | Design/population | Effects | Costs | Outcomes/findings |
|---|---|---|---|---|
| Bolin et al. (2009b) | • BENESCO Markov simulation<br>• Cost-effectiveness and cost-utility analyses<br>• Simulated model in four European countries (Belgium, France, Sweden, and United Kingdom)<br>• Intervention/comparison:<br>– Varenicline<br>– NRT<br>• Perspective: National healthcare system<br>• Lifetime | • Life-years gained<br>• QALYs gained | • Intervention<br>• Morbidity-related healthcare costs from four smoking-related morbidities (lung cancer, COPD, CHD, and stroke)<br>• Base year: Not available<br>• Source: Country-specific databases | • In a typical smoking cessation intervention, using varenicline instead of NRT was cost-saving in all countries except France, which had a cost-effectiveness ratio of $3,936 ($4,981 in 2017 $) per QALY gained |
| Igarashi et al. (2009) | • Markov model<br>• Cost-utility analysis<br>• Simulated cohort of smokers in Japan who started smoking at 20 years of age<br>• Intervention/comparison:<br>– Counseling on smoking cessation by a physician<br>– Counseling plus varenicline therapy<br>• Perspective: Healthcare payer<br>• Lifetime | • QALYs gained | • Treatment<br>• Direct lifetime medical costs for tobacco-associated disease<br>• Base year: 2007<br>• Source: Survey of public health insurance, National Health Insurance, and drug tariff | • Adding varenicline to counseling increased QALYs and saved medical costs among men Adding varenicline to counseling had an incremental cost-effectiveness ratio of $3,010 ($4,075 in 2017 $) per QALY gained in women |
| Knight et al. (2010) | BENESCO Markov simulation<br>Cost-effectiveness and cost-utility analyses<br>Hypothetical population of adult American smokers who made a single quit attempt<br>• Intervention/comparison:<br>– Initial 12 weeks plus additional 12 weeks of varenicline<br>– 12 weeks of varenicline, bupropion, NRT, or unaided cessation<br>• Perspective: Healthcare system<br>• 5, 10, and 20 years and lifetime | • QALYs gained | • Direct treatment<br>• Morbidity-related healthcare costs of smoking-related diseases (lung cancer, stroke, CHD, COPD, and asthma)<br>• Base year: 2005<br>• Source: Literature, prices in 2005 U.S. Red Book | • An additional 12 weeks of varenicline increased 1-year abstinence rates from 23% to 28% (compared with initial 12 weeks of varenicline)<br>• During the lifetime of all participants, an additional 12 weeks of varenicline was cost-effective compared with the initial 12 weeks of varenicline (an incremental cost per QALY gained of $972 ($1,429 in 2017 $)) and was less costly and more effective (dominates) than other alternatives (bupropion, NRT, and unaided cessation) |

*Source:* Table 5 in Ruger and Lazar (2012).

*Notes:* **BENESCO =** benefits of smoking cessation on outcomes; **CHD =** coronary heart disease; **COPD =** chronic obstructive pulmonary disease; **NRT =** nicotine replacement therapy; **QALYs =** quality-adjusted life-years. Estimates converted to 2017 dollars from the base case year (or publication year if no base case year) using the Medical Care part of the Consumer Price Index (all urban consumers).

**Table 5.8 Summary of economic evaluations of brief counseling for smoking cessation**

| Study | Design/population | Effects | Costs | Outcomes/findings |
|---|---|---|---|---|
| Cummings et al. (1989) | • Model: Not available<br>• Cost-effectiveness analysis<br>• Hypothetical group of patients who were smokers and were seen during a routine office visit<br>• Intervention/comparison: Physician counseling patients for 4 minutes during a routine office visit to quit smoking<br>• Perspective: Societal<br>• Time: Not available | • Quit rates<br>• Life-years saved | • Physician time spent counseling<br>• Self-help materials<br>• Base year: 1984<br>• Source: Average cost of physician visit ($30) and cost of materials ($2) | • Brief advice cost $705–$988 ($3,138–$4,397 in 2017 $) per life-year saved for men and $1,204–$2,058 ($5,358–$9,159 in 2017 $) per life-year saved for women |
| Meenan et al. (1998) | • Randomized controlled trial<br>• Cost-effectiveness analysis<br>• Hospitalized adult smokers in two acute-care hospitals in a large group model HMO in Oregon and Washington<br>• Intervention/comparison:<br>– 20-minute bedside counseling session with health counselor, 12-minute video, self-help materials, and one or two follow-up phone calls<br>– Usual care<br>• Perspective: Implementing hospital<br>• 1 year | • Quit rates<br>• Life-years saved | • Intervention (identify patients, deliver counseling, and follow-up)<br>• Base year: 1994<br>• Source: Project surveys, expense reports, retrospective labor estimates, financial staff of HMO, and estimates from literature | • Cost of intervention was $159 ($358 in 2017 $) per smoker<br>• Incremental cost per incremental quit was $3,697 ($8,382 in 2017 $)<br>• Incremental cost per incremental discounted life-year saved was $1,691–$7,444 ($3,809–$16,769 in 2017 $) |
| Haile et al. (2002) | • Cohort<br>• Cost-effectiveness analysis<br>• All smokers attending a noncardiac surgical preadmission clinic in Australia<br>• Intervention/comparison: Structured, interactive computerized smoking cessation program<br>• Perspective: Hospital/payer<br>• 2 months, 1 year | • Quit rates<br>• Acceptability of computerized smoking cessation intervention | • Intervention (developing program, computer hardware, and software)<br>• Base year: Not available (study conducted in 1999)<br>• Source: Invoice | • Costs of intervention at 1 year, by smoking status:<br>– $5.80 ($11.0 in 2017 $) per patient<br>– $24.19 ($45.9 in 2017 $) per smoker<br>– $271.47 ($514.9 in 2017 $) per quitter |

**Table 5.8 Continued**

| Study | Design/population | Effects | Costs | Outcomes/findings |
|---|---|---|---|---|
| Solberg et al. (2006) | • Model: Not available<br>• Cost-utility analysis<br>• Hypothetical group of patients in primary care clinics in the United States<br>• Intervention/comparison:<br>– Model 1: One-time counseling<br>– Model 2: Model 1 plus costs of smoking-attributable illness<br>– Model 3: Annual counseling<br>– Model 4: Model 3 plus costs of smoking-attributable illness<br>• Perspective: Societal<br>• Lifetime | • QALYs | • Intervention (clinician time, medication, and patient time and travel)<br>• Preventable smoking-attributed illness<br>• Base year: 2000<br>• Source: Medicare reimbursement rates, wholesale costs, and healthcare charges | • Cost-effectiveness per QALY saved was $1,100 ($2,005 in 2017 $) for Model 1 and 2,266 ($4,130 in 2017 $) for Model 3<br>• Models 2 and 4 were cost-saving, with net cost savings of $65 ($118 in 2017 $) and $542 ($988 in 2017 $), respectively, per smoker counseled |
| Akers et al. (2007) | • Randomized trial<br>• Cost-effectiveness analysis<br>• Persons in five northern states (Alaska, Idaho, Montana, Oregon, and Washington) who were interested in quitting smokeless tobacco<br>• Intervention/comparison:<br>– Self-help manual only<br>– Assisted self-help (manual plus videotape and two supportive phone calls from a tobacco cessation counselor)<br>• Perspective: Societal and provider/agency 18 months | • Quit rates | • Program (materials, postage, phone services, and counselor and<br>• staff time)<br>• Participants' and supporters' time<br>• Base year: 2000<br>• Source: Cost of materials in bulk and minimum wage in Oregon | • Total cost per participant by perspective and type of treatment:<br>– No treatment:<br>○ Societal: $0 ($0 in 2017 $)<br>○ Provider/agency: $0 ($0 in 2017 $)<br>– Manual only:<br>○ Societal: $20 ($36 in 2017 $)<br>○ Provider/agency: $8 ($15 in 2017 $)<br>– Assisted self-help:<br>○ Societal: $56 ($102 in 2017 $)<br>○ Provider/agency: $39 ($71 in 2017 $)<br>• Incremental cost per quit by perspective and type of treatment:<br>– Manual only:<br>○ Societal: $691 ($1,259 in 2017 $)<br>○ Provider/agency: $481 ($376 in 2017 $)<br>– Assisted self-help:<br>○ Societal: $1,131 ($2,061 in 2017 $)<br>○ Provider/agency: $973 ($1,773 in 2017 $) |

**Table 5.8 Continued**

| Study | Design/population | Effects | Costs | Outcomes/findings |
|---|---|---|---|---|
| Barnett et al. (2008) | • Randomized trial<br>• Cost-effectiveness analysis<br>• Mental health outpatients who were smokers and being treated for depression<br>• Intervention/comparison:<br>– Brief contact (stop-smoking guide and referral list)<br>– Stepped smoking cessation program Perspective: Healthcare payer<br>• 18 months | • Abstinence rates<br>• Life-years gained | • All smoking cessation services used by participants, including intervention and referral<br>• Mental healthcare<br>• Base year: 2003<br>• Source: Retail cost, Medicare reimbursement rates, hospital charge data, and Red Book prices | • Smoking cessation services cost $6,204 ($9,926 in 2017 $) per successful quit or $5,170 ($8,271 in 2017 $) per life-year gained<br>• Cessation services plus mental healthcare cost $11,496 ($18,392 in 2017 $) per successful quit or $9,580 ($15,327 in 2017 $) per life-year gained |
| Dino et al. (2008) | • Markov transition model<br>• Cost-effectiveness analysis<br>• Students 17–25 years of age who smoked ≥5 cigarettes per day and attended selected schools in Florida<br>• Intervention/comparison:<br>– Not On Tobacco (or N-O-T) smoking cessation program<br>– Brief, 20-minute intervention<br>• Perspective: School<br>• 25 years of age | • Quit rates<br>• Life-years saved | • Intervention (training, room and board for trainer, brochures, and gifts)<br>• Base year: 2000<br>• Source: Program and school records | • Incremental cost-effectiveness ratio for N-O-T program was $443 ($807 in 2017 $) per discounted life-year saved in base model: $1,029 ($1,875 in 2017 $) in worst-case scenario<br>$274 ($499 in 2017 $) in best-case scenario |
| Ruger et al. (2008) | • Randomized controlled trial<br>• Cost-effectiveness and cost-utility analyses<br>• Low-income pregnant women in Boston, Massachusetts<br>• Intervention/comparison:<br>– Motivational interviewing with nurse tailored to patient's stage of readiness for cessation<br>– Brief counseling<br>• Perspective: Societal<br>• Lifetime | • QALYs saved<br>• Life-years saved | • Program (intervention, travel, and training)<br>• Neonatal intensive care<br>• Maternal healthcare (cardiovascular and ng diseases)<br>• Base year: 1997<br>• Source: Program records and published estimates | • For smoking cessation, intervention was costlier and less effective than usual care<br>• For relapse prevention, cost-effectiveness of the intervention was $851 ($1,724 in 2017 $) per life-year saved and $628 ($1,272 in 2017 $) per QALY saved |

**Table 5.8 Continued**

| Study | Design/population | Effects | Costs | Outcomes/findings |
|---|---|---|---|---|
| Thavorn and Chaiyakunapruk et al. (2008) | • Markov model<br>• Cost-effectiveness analysis<br>• Two simulated cohorts of Thai smokers—40, 50, and 60 years of age—who regularly smoked 10–20 cigarettes per day<br>• Intervention/comparison:<br>– Structured community pharmacist-based smoking cessation program (personalized and supportive advice, assessment, therapy, self-help material, and follow-up visits)<br>– Usual care (assessment, brief advice and support, and therapy without follow-up care)<br>• Perspective: Healthcare system<br>• Lifetime | • Life-years gained | • Intervention (pharmacist training, fees, and medications)<br>• Direct medical costs of smoking-related diseases (COPD, lung cancer, stroke, and cardiovascular disease)<br>• Base year: 2005<br>• Source: Published studies, information centers, and price index | • In the cohort of those 40 years of age, program resulted in cost savings to the health system of $500 ($735 in 2017 $) for men and $614 ($903 in 2017 $) for women, and 0.18 life-years gained for men and 0.24 life-years gained for women |
| Boyd and Briggs (2009) | Observational study<br>Cost-effectiveness and cost-utility analyses<br>Smokers who accessed either of two cessation services between March and May 2007 in Glasgow, Scotland<br>• Intervention/comparison:<br>– One-to-one cessation support in pharmacies<br>– Group counseling in the community<br>– Self-quit attempt<br>• Perspective: National health system<br>• 4 weeks and 1 year | • Quit rates<br>• QALYs | • Intervention costs incurred by National Health Service (NRT, professional time, overhead, and materials used)<br>• Base year: 2007<br>• Source: Resource use and records from the National Health Service | • Incremental cost per additional 4-week quitter was $1,512 ($2,047 in 2017 $) for pharmacy support and $2,158 ($2,922 in 2017 $) for group counseling in the community compared with self-quit cessation attempts<br>• Incremental cost per QALY gained was $8,620 ($11,671 in 2017 $) for pharmacy services and $10,579 ($14,324 in 2017 $) for group counseling in the community compared with self-quit cessation attempts |

*Source:* Table 6 in Ruger and Lazar (2012).

*Notes:* **COPD =** chronic obstructive pulmonary disease; **HMO =** health maintenance organization; **NRT =** nicotine replacement therapy; **QALYs =** quality-adjusted life-years. Estimates converted to 2017 dollars from the base case year (or publication year if no base case year) using the Medical Care part of the Consumer Price Index (all urban consumers).

that incremental cost-effectiveness ratios ranged from $3,809 to $16,769 per life-year saved compared with usual care from the implementing hospital perspective (Meenan et al. 1998), and another evaluation of stepped cessation services found that ratios per life-year gained ranged from $8,271 to $15,327 compared with brief contact from the healthcare perspective (Barnett et al. 2008). Three evaluations of counseling therapies per additional quit found that the incremental cost-effectiveness ratio was $8,382 from the implementing hospital perspective (Meenan et al. 1998) and that cost-effectiveness ratios ranged from $9,926 to $18,392 from the healthcare perspective (Barnett et al. 2008) and from $1,259 to $2,061 from the societal perspective (Akers et al. 2007). Using an observational design, Boyd and Briggs (2009) found incremental cost-effectiveness ratios per QALY gained of $11,671 for one-to-one support (by a pharmacist) and $14,324 for group counseling, and found incremental cost-effectiveness ratios per quit of $2,047 and $2,922 for one-to-one support and for group counseling, respectively, compared with self-quit cessation attempts from the national health system perspective. In other studies that compared brief counseling or smoking cessation programs with usual care, estimated incremental cost-effectiveness ratios ranged from $499 to $1,875 per life-year saved from the school perspective (Dino et al. 2008), from $735 to $903 from the healthcare perspective (Thavorn and Chaiyakunapruk 2008), and from $3,138 to $9,159 per life-year saved from the societal perspective (Cummings et al. 1989). Additionally, the incremental cost-effectiveness ratio was $4,130 per QALY gained from the societal perspective (Solberg et al. 2006).

### Cost-Effectiveness of Nonclinical Smoking Cessation Interventions

Table 5.9 summarizes studies on the cost-effectiveness of various policy interventions that promote smoking cessation. To standardize the dollar value of costs to the same base year, estimates in this section were converted to 2017 U.S. dollars from the base case year (or publication year if no base case year) using the Medical Care part of the Consumer Price Index (all urban consumers). Although these studies share this focus, the evaluations were highly heterogeneous (Ekpu and Brown 2015). Regardless, some of these evaluations estimated cost-effectiveness ratios similar to or greater than those for clinical smoking cessation interventions. The estimated incremental cost-effectiveness ratios for an NRT program and for a smoke-free workplace policy compared with the clinical standard were $7,736 and $882 per QALY gained, respectively (Ong and Glantz 2005). Villanti and colleagues (2012) evaluated the American Legacy Foundation's national EX campaign, which was a radio and television campaign from 2008 designed to promote smoking cessation among adult smokers. The estimated incremental cost-effectiveness ratios ranged from $47,271 to $102,883 per QALY gained from the societal perspective when compared with a hypothetical status quo of no program or change in cessation behavior. School-based antitobacco education programs compared with status quo have a much wider range of estimated incremental cost-effectiveness ratios per QALY gained over 50 years, ranging from $9,294 when considering a 56% reduction in smoking that dissipates in 4 years to $644,890 when considering a 5% reduction in smoking that dissipates in 1 year from the societal perspective. For the most plausible scenario of 30% effectiveness in preventing smoking, which dissipates in 4 years, the estimated cost-effectiveness ratio was $37,935 per QALY gained (Tengs et al. 2001). In a study evaluating CDC's *Tips From Former Smokers (Tips) Campaign* among adults, Xu and colleagues (2015a) estimated an incremental cost-effectiveness ratio of $450 per life-year saved and $307 per QALY gained in the short run from the funding agency's perspective compared with not having the campaign.

### Cost-Effectiveness of Tobacco Price Increases Through Taxation

Contreary and colleagues (2015) conducted a systematic review of the cost-effectiveness of a tobacco price increase through taxation and found only one study that evaluated the cost-effectiveness per QALY gained. The study found that the cost-effectiveness ratio for a 10% increase in per unit price of tobacco through a 15% increase in excise tax was $3,839 (2017 dollars) per QALY gained over 100 years from the healthcare perspective (van Baal et al. 2007).

## Synthesis of the Evidence

The evidence on cost-effectiveness of smoking cessation and the resulting reduction in healthcare expenditures as a result of cessation strongly indicate that smoking cessation interventions should be implemented throughout the healthcare system and supported more broadly by population-level tobacco control measures (e.g., quitlines). The selection of the intervention depends on the feasibility of the intervention and on the context of an organization and its ability to fund the intervention.

Current estimates of the cost-effectiveness of smoking cessation are limited by the variation in methodologies, including heterogeneity in comparators and perspectives. Despite specific recommendations made two decades ago to enhance the comparability of economic evaluations (Gold et al. 1996), compliance with the full set of recommendations on a standard approach to conducting cost-effective analysis remains incomplete (Ronckers et al. 2005; Ruger and Lazar 2012; Ekpu and

**Table 5.9 Summary of economic evaluations of nonclinical interventions for smoking cessation**

| Study | Design/population | Effects | Costs | Outcomes/findings |
|---|---|---|---|---|
| Tengs et al. (2001) | • Tobacco Policy Model (a dynamic simulation model)<br>• Intervention/comparison:<br>– School-based antitobacco education to seventh- and eighth-grade students, with 5–56% smoking reductions that dissipate in 1–4 years<br>– Status quo<br>• Students 8 years of age and older<br>• Perspective: Societal<br>• 25–50 years | • QALYs | • Costs of school-based antitobacco education program and annual medical costs<br>• Base year: 1999<br>• Source: Salaries of educators for public middle school teachers, average class size, and census data | • Cost-effectiveness ratios per QALY gained over the 50 years ranged from $4,900 ($9,294 in 2017 $), when considering a 56% reduction in smoking that dissipates in 4 years, to $340,000 ($644,890 in 2017 $), when considering a 5% reduction in smoking that dissipates in 1 year<br>• For most plausible scenario of 30% reduction in smoking that dissipates in 4 years, the cost-effectiveness ratio per QALY gained over the 50 years was $20,000 ($37,935 in 2017 $) |
| Ong and Glantz (2005) | • Monte Carlo simulation model<br>• Cost-effectiveness and cost-utility analyses<br>• 18 years of age and older<br>• Interventions/comparison:<br>– A free NRT program and statewide smokefree workplace campaign<br>– Common clinical standard<br>Perspective: Not stated<br>1 year | • Quit rates<br>• QALYs | • Free NRT program: Average wholesale price for NRT, cost of quit attempt, cost of therapy, and cost of total medication; did not include cost of administration<br>• Source: Wholesale prices for the most inexpensive NRTs<br>• Smokefree workplace policy: Costs for enactment and reinforcement<br>• Source: Occupational Employment Statistics Survey and published studies<br>• Base year: 2001 | Free NRT program: Generated 18,500 quitters, and the cost-effectiveness ratios were $7,020 ($12,223 in 2017 $) per quitter and $4,440 ($7,736 in 2017 $) per QALY gained<br>• Smokefree workplace policy: Generated 10,400 quitters, and the cost-effectiveness ratios were $799 ($1,392 in 2017 $) per quitter and $506 ($882 in 2017 $) per QALY gained |

**Table 5.9 Continued**

| Study | Design/population | Effects | Costs | Outcomes/findings |
|---|---|---|---|---|
| Villanti et al. (2012) | • Cost-utility analysis<br>• 18- to 49-year-olds in eight designated markets<br>• Interventions/comparison:<br>– National EX campaign to promote smoking cessation<br>– Status quo<br>• Perspective: Societal<br>• 6 months | • QALYs | • EX campaign costs (media, public relations, salaries, and recruitment) and other societal costs (consumer time and treatment costs)<br>• Base year: 2009<br>• Source: Consumer time lost during exposure to intervention and costs of treatment | • The EX campaign achieved 52,979 additional quit attempts and 4,238 additional quits, and saved 4,450 QALYs<br>• Incremental cost-utility ratios per QALY gained ranged from $37,355 ($47,271 in 2017 $) to $81,301 ($102,883 in 2017 $) |
| Xu et al. (2015a) | • Monte Carlo simulation model<br>• Cost-effectiveness and cost-utility analyses<br>• Quitters, 18 years of age and older<br>• Interventions/comparisons:<br>– Tips Campaign<br>– Without Tips Campaign<br>• Perspective: CDC (funding agency)<br>• 6 months | • Quit rates, premature death, life-years, and QALYs | • Cost of Tips Campaign (development, media placement, and evaluation)<br>• Base year: 2012<br>• Source: CDC Office on Smoking and Health's budget for Tips Campaign | • Prevented 17,109 premature deaths, and saved approximately 179,099 QALYs<br>• Cost-effectiveness ratio was $480 ($550 in 2017 $) per quitter, $2,819 ($3,229 in 2017 $) per premature death averted; $393 ($450 in 2017 $) per life-year saved, and $268 ($307 in 2007 $) per QALY gained |

*Notes:* **NRT =** nicotine replacement therapy; **QALYs =** quality-adjusted life-years; **Tips =** *Tips From Former Smokers Campaign*. Estimates converted to 2017 dollars from the base case year (or publication year if no base case year) using the Medical Care part of the Consumer Price Index (all urban consumers).

Brown 2015). The new recommendations from the second Panel on Cost-Effectiveness in Health and Medicine, which were published after the publication of many of the studies reviewed in this chapter, emphasize the need for compliance with the recommendations for consistency and comparability of studies (Sanders et al. 2016). Additionally, current trends in cigarette smoking and other forms of tobacco product use affect estimates of economic expenditures from smoking and smoking cessation.

Nonetheless, the scientific evidence clearly documents that smoking cessation interventions reduce smoking-attributable expenditures. Evidence on the cost-effectiveness of smoking cessation interventions is consistent across numerous studies—even when considering different methodologies and outcomes.

The evidence from studies of economic burden has shown that cigarette smoking generates substantial smoking-attributable healthcare expenditures and lost productivity, a conclusion reached in previous reports of the Surgeon General (USDHHS 2014). These expenditures affect the smoker specifically and society generally. Using the values per QALY discussed previously (USDHHS 2016), the evidence from economic evaluations that focus on the cost-effectiveness of smoking cessation interventions demonstrates that such interventions are cost-effective from various perspectives and that the cost-effectiveness ratio from the societal perspective will always be higher than from other perspectives. Taken together, the scientific evidence on the health and cost benefits of smoking cessation interventions indicates that these interventions should be implemented as widely as possible throughout the healthcare system and supported more broadly by population-level tobacco control measures.

# Summary of the Evidence

This chapter examines morbidity, mortality, and economic costs in relation to smoking cessation. For general measures of health outcomes, particularly general QoL, there is evidence of higher levels of improvement in QoL among former smokers than among those who continue to smoke. Morbidity is higher in former smokers than in never smokers, but in some subgroups, morbidity among former smokers can approach that of never smokers, such as among those with lower levels of addiction at the time of cessation.

A causal link between smoking cessation and a decrease in general morbidity is supported by the biologic plausibility of the relationship. Many well-supported mechanisms link smoking cessation to improvements in more specific measures of health, such as disease-specific outcomes, thus underscoring the certainty that those who quit smoking will have lower rates of morbidity.

The health benefits of smoking cessation on all-cause mortality have been covered extensively in previous Surgeon General's reports. The evidence that has accumulated since the 1990 Surgeon General's report affirms that smoking cessation at any age reduces the risk of premature death from a smoking-caused illness.

Cigarette smoking generates substantial smoking-attributable healthcare expenditures and lost productivity. These expenditures affect the smoker specifically and society generally. The evidence from economic evaluations that focus on the cost-effectiveness of smoking cessation interventions demonstrates that such interventions are cost-effective from various perspectives. Taken together, the scientific evidence on the health and cost benefits of smoking cessation interventions indicates that these interventions should be implemented as widely as possible throughout the healthcare system and supported more broadly by population-level tobacco control measures.

# Conclusions

1. The evidence is sufficient to infer that smoking cessation improves well-being, including higher quality of life and improved health status.

2. The evidence is sufficient to infer that smoking cessation reduces mortality and increases the lifespan.

3. The evidence is sufficient to infer that smoking exacts a high cost for smokers, healthcare systems, and society.

4. The evidence is sufficient to infer that smoking cessation interventions are cost-effective.

## References[1]

Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, Filiberti A, Flechtner H, Fleishman SB, de Haes JC, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *Journal of the National Cancer Institute* 1993;85(5):365–76.

Akers L, Severson HH, Andrews JA, Lichtenstein E. Cost-effectiveness of self-help smokeless tobacco cessation programs. *Nicotine and Tobacco Research* 2007;9(9):907–14.

An LC, Schillo BA, Kavanaugh AM, Lachter RB, Luxenberg MG, Wendling AH, Joseph AM. Increased reach and effectiveness of a statewide tobacco quitline after the addition of access to free nicotine replacement therapy. *Tobacco Control* 2006;15(4):286–93.

Annemans L, Nackaerts K, Bartsch P, Prignot J, Marbaix S. Cost effectiveness of varenicline in Belgium, compared with bupropion, nicotine replacement therapy, brief counselling and unaided smoking cessation: a BENESCO Markov cost-effectiveness analysis. *Clinical Drug Investigation* 2009;29(10):655–65.

Antoñanzas F, Portillo F. [Economic evaluation of pharmacotherapies for smoking cessation]. *Gaceta Sanitaria* 2003;17(5):393–403.

Baim DS, Cutlip DE, Midei M, Linnemeier TJ, Schreiber T, Cox D, Kereiakes D, Popma JJ, Robertson L, Prince R, et al. Final results of a randomized trial comparing the MULTI-LINK stent with the Palmaz-Schatz stent for narrowings in native coronary arteries. *American Journal of Cardiology* 2001;87(2):157–62.

Baim DS, Cutlip DE, Sharma SK, Ho KK, Fortuna R, Schreiber TL, Feldman RL, Shani J, Senerchia C, Zhang Y, et al. Final results of the Balloon vs. Optimal Atherectomy Trial (BOAT). *Circulation* 1998;97(4):322–31.

Balduyck B, Sardari Nia P, Cogen A, Dockx Y, Lauwers P, Hendriks J, Van Schil P. The effect of smoking cessation on quality of life after lung cancer surgery. *European Journal of Cardio-Thoracic Surgery* 2011;40(6):1432-7; discussion 7-8.

Barnett PG, Wong W, Hall S. The cost-effectiveness of a smoking cessation program for out-patients in treatment for depression. *Addiction* 2008;103(5):834–40.

Bellido-Casado J, Martin-Escudero J, Duenas-Laita A, Mena-Martin FJ, Arzua-Mouronte D, Simal-Blanco F. The SF-36 Questionnaire as a measurement of health-related quality of life: assessing short- and medium-term effects of exposure to tobacco versus the known long-term effects. *European Journal of Internal Medicine* 2004;15(8):511–7.

Bergman B, Aaronson NK, Ahmedzai S, Kaasa S, Sullivan M. The EORTC QLQ-LC13: a modular supplement to the EORTC Core Quality of Life Questionnaire (QLQ-C30) for use in lung cancer clinical trials. EORTC Study Group on Quality of Life. *European Journal of Cancer* 1994;30A(5):635–42.

Bjordal K, Ahlner-Elmqvist M, Tollesson E, Jensen AB, Razavi D, Maher EJ, Kaasa S. Development of a European Organization for Research and Treatment of Cancer (EORTC) questionnaire module to be used in quality of life assessments in head and neck cancer patients. EORTC Quality of Life Study Group. *Acta Oncologica* 1994;33(8):879–85.

Bolin K, Lindgren B, Willers S. The cost utility of bupropion in smoking cessation health programs: simulation model results for Sweden. *Chest* 2006;129(3):651–60.

Bolin K, Mork AC, Wilson K. Smoking-cessation therapy using varenicline: the cost-utility of an additional 12-week course of varenicline for the maintenance of smoking abstinence. *Journal of Evaluation in Clinical Practice* 2009a;15(3):478–85.

Bolin K, Wilson K, Benhaddi H, de Nigris E, Marbaix S, Mork AC, Aubin HJ. Cost-effectiveness of varenicline compared with nicotine patches for smoking cessation—results from four European countries. *European Journal of Public Health* 2009b;19(6):650–4.

Bolliger CT, Zellweger JP, Danielsson T, van Biljon X, Robidou A, Westin Å, Perruchoud AP, Säwe U. Smoking reduction with oral nicotine inhalers: double blind, randomised clinical trial of efficacy and safety. *BMJ* 2000;321(7257):329–33.

Bolliger CT, Zellweger JP, Danielsson T, van Biljon X, Robidou A, Westin Å, Perruchoud AP, Säwe U. Influence of long-term smoking reduction on health risk markers and quality of life. *Nicotine and Tobacco Research* 2002;4(4):433–9.

Boyd KA, Briggs AH. Cost-effectiveness of pharmacy and group behavioural support smoking cessation services in Glasgow. *Addiction* 2009;104(2):317–25.

Centers for Disease Control and Prevention. Smoking-attributable mortality, years of potential life lost, and productivity losses—United States, 2000–2004. *Morbidity and Mortality Weekly Report* 2008;57(45):1226–8.

Centers for Disease Control and Prevention. Cigarette smoking—United States, 1965–2008. *Morbidity*

[1]For reference entries that contain URLs, those URLs were active on the access date presented in the respective reference entry.

*and Mortality Weekly Report Supplements* 2011;60(01):109–13.

Centers for Disease Control and Prevention. *Best Practices for Comprehensive Tobacco Control Programs—2014*. Atlanta (GA): U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2014; <https://www.cdc.gov/tobacco/stateandcommunity/best_practices/pdfs/2014/comprehensive.pdf>; accessed: July 26, 2017.

Chaloupka FJ, Warner KE. The Economics of Smoking. In: Culyer AJ, Newhouse JP, editors. *Handbook of Health Economics,* 1B. Amsterdam: Elsevier North Holland, 2000.

Cohen DJ, Reynolds MR. Interpreting the results of cost-effectiveness studies. *Journal of the American College of Cardiology* 2008;52(25):2119–26.

Contreary KA, Chattopadhyay SK, Hopkins DP, Chaloupka FJ, Forster JL, Grimshaw V, Holmes CB, Goetzel RZ, Fielding JE. Economic impact of tobacco price increases through taxation: a Community Guide systematic review. *American Journal of Preventive Medicine* 2015;49(5):800–8.

Cornuz J, Gilbert A, Pinget C, McDonald P, Slama K, Salto E, Paccaud F. Cost-effectiveness of pharmacotherapies for nicotine dependence in primary care settings: a multinational comparison. *Tobacco Control* 2006;15(3):152–9.

Crealey GE, McElnay JC, Maguire TA, O'Neill C. Costs and effects associated with a community pharmacy-based smoking-cessation programme. *Pharmacoeconomics* 1998;14(3):323–33.

Croghan IT, Schroeder DR, Hays JT, Eberman KM, Patten CA, Berg EJ, Hurt RD. Nicotine dependence treatment: perceived health status improvement with 1-year continuous smoking abstinence. *European Journal of Public Health* 2005;15(3):251–5.

Cromwell J, Bartosch WJ, Fiore MC, Hasselblad V, Baker T. Cost-effectiveness of the clinical practice recommendations in the AHCPR guideline for smoking cessation. *JAMA: the Journal of the American Medical Association* 1997;278(21):1759–66.

Cummings SR, Rubin SM, Oster G. The cost-effectiveness of counseling smokers to quit. *JAMA: the Journal of the American Medical Association* 1989;261(1):75–9.

Dino G, Horn K, Abdulkadri A, Kalsekar I, Branstetter S. Cost-effectiveness analysis of the Not On Tobacco program for adolescent smoking cessation. *Prevention Science* 2008;9(1):38–46.

Ekpu VU, Brown AK. The economic impact of smoking and of reducing smoking prevalence: review of evidence. *Tobacco Use Insights* 2015;8:1–35.

Erickson SR, Thomas LA, Blitz SG, Pontius LR. Smoking cessation: a pilot study of the effects on health-related quality of life and perceived work performance one week into the attempt. *Annals of Pharmacotherapy* 2004;38(11):1805–10.

Feenstra TL, Hamberg-van Reenen HH, Hoogenveen RT, Rutten-van Mölken MP. Cost-effectiveness of face-to-face smoking cessation interventions: a dynamic modeling study. *Value in Health* 2005;8(3):178–90.

Fellows JL, Bush T, McAfee T, Dickerson J. Cost effectiveness of the Oregon quitline "free patch initiative". *Tobacco Control* 2007;16(Suppl 1):i47–i52.

Fiscella K, Franks P. Cost-effectiveness of the transdermal nicotine patch as an adjunct to physicians' smoking cessation counseling. *JAMA: the Journal of the American Medical Association* 1996;275(16):1247–51.

Frisch MB, Cornell J, Villanueva M, Retzlaff PJ. Clinical validation of the Quality of Life Inventory: a measure of life satisfaction for use in treatment planning and outcome assessment. *Psychological Assessment* 1992;4:92–101.

Gilbert AR, Pinget C, Bovet P, Cornuz J, Shamlaye C, Paccaud F. The cost effectiveness of pharmacological smoking cessation therapies in developing countries: a case study in the Seychelles. *Tobacco Control* 2004;13(2):190–5.

Gold MR, Siegel JE, Russell LB, Weinstein MC, editors. *Cost-Effectiveness in Health and Medicine*. New York: Oxford University Press, 1996.

Goldenberg M, Danovitch I, IsHak WW. Quality of life and smoking. *American Journal on Addictions* 2014;23(6):540–62.

Gruber J. Smoking's internalities. *Regulation* 2002–2003;Winter:52–7.

Gruber J, Koszegi B. Is addiction "rational"? Theory and evidence. *Quarterly Journal of Economics* 2001;116:1261–1303.

Gutiérrez-Bedmar M, Seguí-Gómez M, Gómez-Gracia E, Bes-Rastrollo M, Martínez-González MA. Smoking status, changes in smoking status and health-related quality of life: findings from the SUN ("Seguimiento Universidad de Navarra") cohort. *International Journal of Environmental Research and Public Health* 2009;6(1):310–20.

Haddix AC, Teutsch SM, Corso PS, editors. *Prevention Effectiveness: A Guide to Decision Analysis and Economic Evaluation.* 2nd ed. New York (NY): Oxford University Press, 2003.

Haile MJ, Wiggers JH, Spigelman AD, Knight J, Considine RJ, Moore K. Novel strategy to stop cigarette smoking by surgical patients: pilot study in a preadmission clinic. *ANZ Journal of Surgery* 2002;72(9):618–22.

Halpern MT, Dirani R, Schmier JK. The cost effectiveness of varenicline for smoking cessation. *Managed Care Interface* 2007;20(10):18–25.

Hays JT, Croghan IT, Baker CL, Cappelleri JC, Bushmakin AG. Changes in health-related quality of life with smoking cessation treatment. *European Journal of Public Health* 2012;22(2):224–9.

Hays RD, Morales LS. The RAND-36 measure of health-related quality of life. *Annals of Medicine* 2001;33(5):350–7.

Heatherton TF, Kozlowski LT, Frecker RC, Fagerström KO. The Fagerström test for nicotine dependence: a revision of the Fagerström Tolerance Questionnaire. *British Journal of Addiction* 1991;86(9):1119–27.

Heikkinen H, Jallinoja P, Saarni SI, Patja K. The impact of smoking on health-related and overall quality of life: a general population survey in Finland. *Nicotine and Tobacco Research* 2008;10(7):1199–207.

Hollis JF, McAfee TA, Fellows JL, Zbikowski SM, Stark M, Riedlinger K. The effectiveness and cost effectiveness of telephone counselling and the nicotine patch in a state tobacco quitline. *Tobacco Control* 2007;16(Suppl 1):i53–i59.

Hoogendoorn M, Welsing P, Rutten-van Mölken MP. Cost-effectiveness of varenicline compared with bupropion, NRT, and nortriptyline for smoking cessation in the Netherlands. *Current Medical Research and Opinion* 2008;24(1):51–61.

Howard P, Knight C, Boler A, Baker C. Cost-utility analysis of varenicline versus existing smoking cessation strategies using the BENESCO simulation model: application to a population of U.S. adult smokers. *Pharmacoeconomics* 2008;26(6):497–511.

Igarashi A, Takuma H, Fukuda T, Tsutani K. Cost-utility analysis of varenicline, an oral smoking-cessation drug, in Japan. *Pharmacoeconomics* 2009;27(3):247–61.

Jackson KC 2nd, Nahoopii R, Said Q, Dirani R, Brixner D. An employer-based cost-benefit analysis of a novel pharmacotherapy agent for smoking cessation. *Journal of Occupational and Environmental Medicine* 2007;49(4):453–60.

Jensen K, Jensen AB, Grau C. Smoking has a negative impact upon health related quality of life after treatment for head and neck cancer. *Oral Oncology* 2007;43(2):187–92.

Jette AM, Davies AR, Cleary PD, Calkins DR, Rubenstein LV, Fink A, Kosecoff J, Young RT, Brook RH, Delbanco TL. The Functional Status Questionnaire: reliability and validity when used in primary care. *Journal of General Internal Medicine* 1986;1(3):143–9.

Jha P, Chaloupka FJ, Moore J, Gajalakshmi V, Gupta PC, Peck R, Asma S, Zatonski W. Chapter 46: tobacco addiction. In: Jamison DT, Breman JG, Measham AR, Alleyne G, Claeson M, Evans DB, et al., editors. *Disease Control Priorities in Developing Countries*. 2nd ed. Washington (DC): The International Bank for Reconstruction and Development/The World Bank Group, 2006.

Jha P, Ramasundarahettige C, Landsman V, Rostron B, Thun M, Anderson RN, McAfee T, Peto R. 21st-century hazards of smoking and benefits of cessation in the United States. *New England Journal of Medicine* 2013;368(4):341–50.

Knight C, Howard P, Baker CL, Marton JP. The cost-effectiveness of an extended course (12+12 weeks) of varenicline compared with other available smoking cessation strategies in the United States: an extension and update to the BENESCO model. *Value in Health* 2010;13(2):209–14.

Max W, Sung HY, Shi Y, Stark B. The cost of smoking in California. *Nicotine and Tobacco Research* 2016;18(5):1222–9.

McClave AK, Dube SR, Strine TW, Mokdad AH. Associations between health-related quality of life and smoking status among a large sample of U.S. adults. *Preventive Medicine* 2009;48(2):173–9.

Meenan RT, Stevens VJ, Hornbrook MC, La Chance PA, Glasgow RE, Hollis JF, Lichtenstein E, Vogt TM. Cost-effectiveness of a hospital-based smoking cessation intervention. *Medical Care* 1998;36(5):670–8.

Mitra M, Chung MC, Wilber N, Klein Walker D. Smoking status and quality of life: a longitudinal study among adults with disabilities. *American Journal of Preventive Medicine* 2004;27(3):258–60.

Mody RR, Smith MJ. Smoking status and health-related quality of life: as findings from the 2001 Behavioral Risk Factor Surveillance System data. *American Journal of Health Promotion* 2006;20(4):251–8.

Morgan MB, Crayford T, Murrin B, Fraser SC. Developing the Vascular Quality of Life Questionnaire: a new disease-specific quality of life measure for use in lower limb ischemia. *Journal of Vascular Surgery* 2001;33(4):679–87.

Moriarty DG, Zack MM, Kobau R. The Centers for Disease Control and Prevention's Healthy Days Measures—population tracking of perceived physical and mental health over time. *Health and Quality of Life Outcomes* 2003;1:37.

Mulder I, Tijhuis M, Smit HA, Kromhout D. Smoking cessation and quality of life: the effect of amount of smoking and time since quitting. *Preventive Medicine* 2001;33(6):653–60.

National Cancer Institute, World Health Organization. *The Economics of Tobacco and Tobacco Control*. National Cancer Institute Tobacco Control Monograph 21. Bethesda (MD): U.S. Department of Health and Human Services, National Institutes of Health, National Cancer

Institute; and World Health Organization, 2016. NIH Publication No. 16-CA-8029A.

Neumann PJ, Cohen JT, Weinstein MC. Updating cost-effectiveness—the curious resilience of the $50,000-per-QALY threshold. *New England Journal of Medicine* 2014;371(9):796–7.

Office of Disease Prevention and Health Promotion. Health-related quality of life and well-being, April 13, 2018; <https://www.healthypeople.gov/2020/about/foundation-health-measures/Health-Related-Quality-of-Life-and-Well-Being>; accessed: April 16, 2018.

Olufade AO, Shaw JW, Foster SA, Leischow SJ, Hays RD, Coons SJ. Development of the Smoking Cessation Quality of Life questionnaire. *Clinical Therapeutics* 1999;21(12):2113–30.

Ong MK, Glantz SA. Free nicotine replacement therapy programs vs implementing smoke-free workplaces: a cost-effectiveness comparison. *American Journal of Public Health* 2005;95(6):969–75.

Oster G, Huse DM, Delea TE, Colditz GA. Cost-effectiveness of nicotine gum as an adjunct to physician's advice against cigarette smoking. *JAMA: the Journal of the American Medical Association* 1986;256(10):1315–8.

Papadopoulos G, Vardavas CI, Limperi M, Linardis A, Georgoudis G, Behrakis P. Smoking cessation can improve quality of life among COPD patients: validation of the clinical COPD questionnaire into Greek. *BMC Pulmonary Medicine* 2011;11:13.

Piper ME, Kenford S, Fiore MC, Baker TB. Smoking cessation and quality of life: changes in life satisfaction over 3 years following a quit attempt. *Annals of Behavioral Medicine* 2012;43(2):262–70.

Pirie K, Peto R, Reeves GK, Green J, Beral V. The 21st century hazards of smoking and benefits of stopping: a prospective study of one million women in the UK. *Lancet* 2013;381(9861):133–41.

Ronckers ET, Groot W, Ament AJ. Systematic review of economic evaluations of smoking cessation: standardizing the cost-effectiveness. *Medical Decision Making* 2005;25(4):437–48.

Ruger JP, Lazar CM. Economic evaluation of pharmaco- and behavioral therapies for smoking cessation: a critical and systematic review of empirical research. *Annual Review of Public Health* 2012;33:279–305.

Ruger JP, Weinstein MC, Hammond SK, Kearney MH, Emmons KM. Cost-effectiveness of motivational interviewing for smoking cessation and relapse prevention among low-income pregnant women: a randomized controlled trial. *Value in Health* 2008;11(2):191–8.

Rungruanghiranya S, Ekpanyaskul C, Hattapornsawan Y, Tundulawessa Y. Effect of nicotine polyestex gum on smoking cessation and quality of life. *Journal of the Medical Association of Thailand* 2008;91(11):1656–62.

Russell LB. The science of making better decisions about health. In: *Population Health: Behavioral and Social Science Insights*. Rockville (MD): Agency for Healthcare Research and Quality, 2015; <http://www.ahrq.gov/professionals/education/curriculum-tools/population-health/russell.html>; accessed: March 15, 2019.

Russell LB, Gold MR, Siegel JE, Daniels N, Weinstein MC. The role of cost-effectiveness analysis in health and medicine. Panel on Cost-Effectiveness in Health and Medicine. *JAMA: the Journal of the American Medical Association* 1996;276(14):1172–7.

Salize HJ, Merkel S, Reinhard I, Twardella D, Mann K, Brenner H. Cost-effective primary care-based strategies to improve smoking cessation: more value for money. *Archives of Internal Medicine* 2009;169(3):230–5.

Sanders GD, Neumann PJ, Basu A, Brock DW, Feeny D, Krahn M, Kuntz KM, Meltzer DO, Owens DK, Prosser LA, et al. Recommendations for conduct, methodological practices, and reporting of cost-effectiveness analyses: Second Panel on Cost-Effectiveness in Health and Medicine. *JAMA: the Journal of the American Medical Association* 2016;316(10):1093–103.

Schumacher M, Rücker G, Schwarzer G. Meta-analysis and the Surgeon General's report on smoking and health. *New England Journal of Medicine* 2014;370(2):186–8.

Shultz JM, Novotny TE, Rice DP. Quantifying the disease impact of cigarette smoking with SAMMEC II software. *Public Health Reports* 1991;106(3):326–33.

Siegel JE, Weinstein MC, Russell LB, Gold MR. Recommendations for reporting cost-effectiveness analyses. Panel on Cost-Effectiveness in Health and Medicine. *JAMA: the Journal of the American Medical Association* 1996;276(16):1339–41.

Sintonen H. *The 15D-measure of health-related quality of life. II. Feasibility, reliability and validity of its valuation system.* Working Paper 42. Melbourne (Australia): National Centre for Health Program Evaluation, 1995.

Skevington SM, Lotfy M, O'Connell KA. The World Health Organization's WHOQOL-BREF quality of life assessment: psychometric properties and results of the international field trial. A report from the WHOQOL group. *Quality of Life Research* 2004;13(2):299–310.

Sloan FA, Ostermann J, Picone G, Conover C, Taylor DH Jr. *The Price of Smoking.* Cambridge (MA): The MIT Press, 2004.

Solberg LI, Maciosek MV, Edwards NM, Khanchandani HS, Goodman MJ. Repeated tobacco-use screening and intervention in clinical practice: health impact and cost effectiveness. *American Journal of Preventive Medicine* 2006;31(1):62–71.

Song F, Raftery J, Aveyard P, Hyde C, Barton P, Woolacott N. Cost-effectiveness of pharmacological interventions for smoking cessation: a literature review and a decision analytic analysis. *Medical Decision Making* 2002;22(5 Suppl):S26–S37.

Stapleton JA, Lowin A, Russell MA. Prescription of transdermal nicotine patches for smoking cessation in general practice: evaluation of cost-effectiveness. *Lancet* 1999;354(9174):210–5.

Stewart AL, King AC, Killen JD, Ritter PL. Does smoking cessation improve health-related quality-of-life? *Annals of Behavioral Medicine* 1995;17(4):331–8.

Stofmeel MA, Post MW, Kelder JC, Grobbee DE, van Hemel NM. Psychometric properties of Aquarel. a disease-specific quality of life questionnaire for pacemaker patients. *Journal of Clinical Epidemiology* 2001;54(2):157–65.

Taira DA, Seto TB, Ho KK, Krumholz HM, Cutlip DE, Berezin R, Kuntz RE, Cohen DJ. Impact of smoking on health-related quality of life after percutaneous coronary revascularization. *Circulation* 2000;102(12):1369–74.

Tengs TO, Osgood ND, Chen LL. The cost-effectiveness of intensive national school-based anti-tobacco education: results from the tobacco policy model. *Preventive Medicine* 2001;33(6):558–70.

Thavorn K, Chaiyakunapruk N. A cost-effectiveness analysis of a community pharmacist-based smoking cessation programme in Thailand. *Tobacco Control* 2008;17(3):177–82.

The EuroQol Group. EuroQol—a new facility for the measurement of health-related quality of life. *Health Policy* 1990;16(3):199–208.

Thun MJ, Carter BD, Feskanich D, Freedman ND, Prentice R, Lopez AD, Hartge P, Gapstur SM. 50-year trends in smoking-related mortality in the United States. *New England Journal of Medicine* 2013;368(4):351–64.

Tian J, Venn AJ, Blizzard L, Patton GC, Dwyer T, Gall SL. Smoking status and health-related quality of life: a longitudinal study in young adults. *Quality of Life Research* 2016;25(3):669–85.

Tillmann M, Silcock J. A comparison of smokers' and ex-smokers' health-related quality of life. *Journal of Public Health Medicine* 1997;19(3):268–73.

Tran MT, Holdford DA, Kennedy DT, Small RE. Modeling the cost-effectiveness of a smoking-cessation program in a community pharmacy practice. *Pharmacotherapy* 2002;22(12):1623–31.

U.S. Bureau of Labor Statistics. Consumer Price Index, 2017; <https://www.bls.gov/cpi/tables/home.htm>; accessed: July 16, 2019.

U.S. Department of Health, Education, and Welfare. *Smoking and Health: Report of the Advisory Committee to the Surgeon General of the Public Health Service.* Washington: U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, 1964. PHS Publication No. 1103.

U.S. Department of Health, Education, and Welfare. *The Health Consequences of Smoking. 1969 Supplement to the 1967 Public Health Service Review.* Washington: U.S. Department of Health, Education, and Welfare, Public Health Service, 1969. DHEW Publication No. 1696-2.

U.S. Department of Health, Education, and Welfare. *Smoking and Health. A Report of the Surgeon General.* Washington: U.S. Department of Health, Education, and Welfare, Office of the Assistant Secretary for Health, Office on Smoking and Health, 1979. DHEW Publication No. (PHS) 79-50066.

U.S. Department of Health and Human Services. *Reducing the Health Consequences of Smoking: 25 Years of Progress. A Report of the Surgeon General.* Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 1989. DHHS Publication No. (CDC) 89-8411.

U.S. Department of Health and Human Services. *The Health Benefits of Smoking Cessation: A Report of the Surgeon General.* Rockville (MD): U.S. Department of Health and Human Services, Centers for Disease Control, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 1990. DHHS Publication No. (CDC) 90-8416.

U.S. Department of Health and Human Services. *The Health Consequences of Smoking: A Report of the Surgeon General.* Atlanta (GA): U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2004.

U.S. Department of Health and Human Services. *Ending the Tobacco Epidemic: A Tobacco Control Strategic Action Plan for the U.S. Department of Health and Human Services.* Washington (DC): Office of the Assistant Secretary for Health, 2010.

U.S. Department of Health and Human Services. *The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General.* Atlanta (GA): U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2014.

U.S. Department of Health and Human Services. *Guidelines for Regulatory Impact Analysis,* 2016; <https://aspe.hhs.gov/system/files/pdf/242926/HHS_RIAGuidance.pdf>; accessed: December 10, 2019.

van Baal PH, Brouwer WB, Hoogenveen RT, Feenstra TL. Increasing tobacco taxes: a cheap tool to increase public health. *Health Policy* 2007;82(2):142–52.

van der Molen T, Willemse BW, Schokker S, ten Hacken NH, Postma DS, Juniper EF. Development, validity and responsiveness of the Clinical COPD Questionnaire. *Health and Quality of Life Outcomes* 2003;1:13.

Velicer WF, Prochaska JO, Rossi JS, Snow MG. Assessing outcome in smoking cessation studies. *Psychological Bulletin* 1992;111(1):23–41.

Villanti AC, Curry LE, Richardson A, Vallone DM, Holtgrave DR. Analysis of media campaign promoting smoking cessation suggests it was cost-effective in prompting quit attempts. *Health Affairs* 2012;31(12):2708–16.

Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Medical Care* 1992;30(6):473–83.

Wasley MA, McNagny SE, Phillips VL, Ahluwalia JS. The cost-effectiveness of the nicotine transdermal patch for smoking cessation. *Preventive Medicine* 1997;26(2):264–70.

Weinstein MC, Siegel JE, Gold MR, Kamlet MS, Russell LB. Recommendations of the Panel on Cost-effectiveness in Health and Medicine. *JAMA: the Journal of the American Medical Association* 1996;276(15):1253–8.

West R, Raw M, McNeill A, Stead L, Aveyard P, Bitton J, Stapleton J, McRobbie H, Pokhrel S, Lester-George A, et al. Health-care interventions to promote and assist tobacco cessation: a review of efficacy, effectiveness and affordability for use in national guideline development. *Addiction* 2015;110(9):1388–403.

Wiggers LC, Oort FJ, Peters RJ, Legemate DA, de Haes HC, Smets EM. Smoking cessation may not improve quality of life in atherosclerotic patients. *Nicotine and Tobacco Research* 2006;8(4):581–9.

Wilber N, Mitra M, Walker DK, Allen D, Meyers AR, Tupper P. Disability as a public health issue: findings and reflections from the Massachusetts Survey of Secondary Conditions. *Milbank Quarterly* 2002;80(2):393–421.

Xu X, Alexander RL Jr, Simpson SA, Goates S, Nonnemaker JM, Davis KC, McAfee T. A cost-effectiveness analysis of the first federally funded antismoking campaign. *American Journal of Preventive Medicine* 2015a;48(3):318–25.

Xu X, Bishop EE, Kennedy SM, Simpson SA, Pechacek TF. Annual healthcare spending attributable to cigarette smoking: an update. *American Journal of Preventive Medicine* 2015b;48(3):326–33.

Zillich AJ, Ryan M, Adams A, Yeager B, Farris K. Effectiveness of a pharmacist-based smoking-cessation program and its impact on quality of life. *Pharmacotherapy* 2002;22(6):759–65.