

# Emerging Issues in Smoking Among Adolescent and Adult Cancer Survivors

## *A Comprehensive Review*

James L. Klosky, PhD<sup>1</sup>

Vida L. Tyc, PhD<sup>1,2</sup>

Danette M. Garces-Webb, MS<sup>1,3</sup>

Joanna Buscemi, BS<sup>1,3</sup>

Robert C. Klesges, PhD<sup>4,5</sup>

Melissa M. Hudson, MD<sup>2,4,6</sup>

<sup>1</sup> Division of Behavioral Medicine, St. Jude Children's Research Hospital, Memphis, Tennessee.

<sup>2</sup> Department of Pediatrics, University of Tennessee Health Science Center, Memphis, Tennessee.

<sup>3</sup> Department of Psychology, University of Memphis, Memphis, Tennessee.

<sup>4</sup> Departments of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Memphis, Tennessee.

<sup>5</sup> Department of Preventive Medicine, University of Tennessee Health Science Center, Memphis, Tennessee.

<sup>6</sup> Department of Oncology, St. Jude Children's Research Hospital, Memphis, Tennessee.

Funded in part by the Cancer Center Support (CORE) Grant CA21765 and the American Lebanese Syrian Associated Charities (ALSAC).

Address for reprints: James L. Klosky, PhD, Division of Behavioral Medicine, St. Jude Children's Research Hospital, 332 N. Lauderdale, Memphis, TN 38105-2794; Fax: (901) 495-4701; E-mail: james.klosky@stjude.org

Received April 19, 2007; revision received May 31, 2007; accepted June 1, 2007.

The number of cancer survivors is significantly increasing, thereby prioritizing the importance of identifying and preventing adverse health outcomes within this high-risk population. Cigarette smoking is of particular salience as it places both adolescents and adults with a cancer history at risk for various health problems, including second malignancies. The purpose of this article is to provide a comprehensive review of the smoking literature as it relates to adolescents and adults on-treatment and surviving cancer. In particular, the article reviews the prevalence, risk factors, and health outcomes associated with smoking, in addition to the prevention and smoking cessation interventions available to adolescent and adult oncology patients. Furthermore, efficacious cessation strategies have recently emerged from the smoking literature in healthy populations, and their application to oncology populations is discussed. *Cancer* 2007;110:2408–19. © 2007 American Cancer Society.

**KEYWORDS:** smoking, oncology patients, risk factors, cancer survivors.

Cigarette smoking is the number 1 preventable cause of morbidity and mortality in the U.S., and despite large public health efforts, nearly 21% of the population still smokes.<sup>1</sup> In addition to targeting adolescent and adult populations for prevention and intervention efforts in general, particular interest has been placed on aggressively targeting those at greater medical risk for smoking-related diseases.<sup>2</sup> Two such high-risk groups include adolescents and adults receiving treatment and surviving cancer. In 2000, the National Cancer Institute estimated that there were approximately 10 million cancer survivors in the U.S. Currently, the 5-year cure rate for pediatric cancers exceeds 75% and outcomes for adult patients are improving as well.<sup>3</sup> As a result, the number of cancer survivors is dramatically increasing, thus prioritizing the importance of identifying efficacious prevention and smoking cessation programs.

The purpose of this article is to provide a comprehensive review of the smoking literature as it relates to adolescents and adults on-treatment and surviving cancer, and to highlight tobacco findings emerging from healthy populations and apply them to patient care issues within the cancer context. The first goal of this review is to examine the prevalence of smoking among cancer patients. Second, the adverse health outcomes associated with smoking within the context of cancer treatment and survival will be addressed, followed by a description of the established and emerging factors associated with smoking. Empirically supported treatments for smoking

prevention and cessation in cancer survivors will be discussed, along with a review of the emerging areas that may eventually be promising smoking cessation components. Finally, limitations and directions for future research are highlighted, followed by suggestions for clinician-based interventions. This review addresses the above issues in adolescents with cancer and adult-onset cancer survivors separately. This is necessary because tobacco control efforts in adolescents with cancer generally focus on smoking prevention, while the literature on adult cancer survivors focuses primarily on cessation.

### **Adolescents Receiving Treatment and Surviving Cancer** *Smoking prevalence*

Although 23% of high school students are current smokers, self-reported rates of smoking among adolescents receiving treatment and surviving cancer appear to be significantly lower.<sup>4</sup> Mulhern et al.<sup>5</sup> first reported that 8.2% of adolescent survivors of childhood cancer used tobacco. Other studies based on self-reports found that 2% to 14% of adolescents with a history of cancer engage in cigarette smoking.<sup>6,7</sup> In what to our knowledge is the only study to date to examine tobacco use in preadolescents, Tyc et al. (unpublished data) found no differences in tobacco use among children ages 8 to 11 years with and without cancer, with zero reports of tobacco use being endorsed among the preadolescent patients. (See Limitations and Future Directions for a discussion on threats to the validity of self-reported smoking in this population.)

### *Adverse health outcomes associated with tobacco use*

Early health consequences for young smokers generally include respiratory symptoms and infections, reduced rates of lung growth and function, increased cough and phlegm production, compromised physical activity, and adverse changes in lipid profiles resulting in cardiovascular sequelae.<sup>8</sup> High school students who regularly smoked for at least 4 years are 2.4 times more likely to report poor overall health and up to 2.7 times more likely to report wheezing or gasping, cough with phlegm or blood, and shortness of breath when not exercising, as compared with their nonsmoking peers.<sup>9</sup> These tobacco-related complications may be particularly damaging for adolescents who are receiving treatment for cancer. For example, acute complications of smoking include predisposition to respiratory infections due to compromised mucosal defenses and increased symptoms of acute radiation mucositis. These complications

may be especially problematic for those patients who are immunocompromised due to cancer treatment. Smoking may also delay rates of healing after surgery, thus compromising rehabilitation efforts and return of the patients' optimal daily functioning.<sup>10</sup>

Adolescents with a history of cancer are already at higher risk for developing smoking-related complications (including second cancers); thus, the long-term sequelae of smoking must also be considered. For example, antineoplastic therapies are associated with future cardiopulmonary toxicities and organ compromise that can be potentiated by smoking.<sup>11</sup> Specifically, patients treated with carmustine and bleomycin and/or pulmonary radiotherapy (RT) are more likely to develop serious respiratory problems and restrictive lung disease if they smoke.<sup>12,13</sup> Likewise, long-term smoking for patients treated with anthracyclines is associated with higher risk of congestive heart failure.<sup>14</sup> RT and smoking are independently associated with decreases in bone density; therefore, the cumulative effect of RT and smoking may place these patients at high risk for osteoporosis.<sup>15</sup> Emphasis must be placed on preventing smoking so that the aforementioned health complications can be avoided in this high-risk group.

### *Emerging issues in smoking-related risk factors in adolescents with a cancer history*

Compared with the literature concerning healthy adolescents, factors influencing tobacco use among adolescents with a history of cancer have received little attention. Yet current research suggests that the sociodemographic and cognitive-motivational variables predictive of tobacco use are similar to those of healthy youths. For example, Tyc et al.<sup>6</sup> compared 90 patients receiving treatment for cancer with 279 healthy adolescents with regard to factors such as intentions to smoke, instrumental value (ie, the relative value associated with smoking), tobacco knowledge (ie, knowledge of the risks associated with tobacco use), perceived vulnerability (ie, the extent to which one believes he/she is vulnerable to tobacco-related health risks), etc. Although nonsmoking adolescents with cancer were one-third less likely to report intentions to smoke, no other significant differences were identified between groups. With regard to adolescents surviving cancer, older age, past tobacco use, lower tobacco knowledge, and greater perceived value of smoking have been found to predict increased intentions of future tobacco use, which is similar to the findings in nonsmoking healthy adolescents.<sup>16,17</sup> These results suggest that smoking prevention and cessation

interventions currently developed for healthy adolescents should generalize to adolescents with a history of cancer.

**Genotyping.** In addition to sociodemographic and psychosocial factors, smoking initiation, age at smoking onset, and smoking escalation may be associated with genetic variation of the dopamine pathway.<sup>18</sup> Support for this theory has developed from studies linking smoking behavior with dopamine receptor and transporter genes, specifically the *A1* and *B1* alleles of the *DRD2* gene and the 10-repeat allele of the *SLC6A3* gene.<sup>19,20</sup> The 9-repeat allele, *SLC6A3*, for example, has been associated with a 22% reduction in dopamine transporter protein, resulting in less clearance and greater bioavailability of dopamine. Thus, individuals who carry the more common 10-repeat allele may achieve greater reward from nicotine's effects on dopamine activity. Because DNA-based tests for susceptibility to nicotine addiction have been developed, we may soon be in a position to accurately predict which individuals will become nicotine-dependent, which has enormous implications for identifying and targeting high-risk patients for smoking prevention before nicotine exposure. This tobacco-control approach is particularly promising in that 61% of adolescents with a history of cancer report interest in undergoing nicotine-addiction susceptibility genetic testing.<sup>21</sup>

**Psychological distress.** Psychologic distress is a well-established factor that influences smoking among adolescents. Regular adolescent smokers are reported to be 3 times more likely to have seen a physician for psychologic complaints compared with their nonsmoking peers.<sup>9</sup> The correlation is even more pronounced among those adolescents genetically predisposed for nicotine addiction. Specifically, Audrain-McGovern et al.<sup>22</sup> found a multiplicative effect of nicotine-addiction genetic polymorphisms and affective distress, with smoking progression being most extreme among those adolescents who were both depressed and genetically susceptible for smoking. The proposed mechanism explaining this correlation lies in the direct pharmacologic effects of nicotine, which reportedly moderates psychologic distress.<sup>23</sup> Although the findings are mixed, evidence suggests that survivors of childhood cancer experience greater levels of psychologic distress in adolescence and young adulthood than do unrelated or sibling controls, thus placing them at high risk for smoking onset and progression.<sup>24</sup>

**Inattention.** Associations between tobacco use and inattention have been well documented among those experiencing attention deficit/hyperactivity disorder (ADHD).<sup>25</sup> Survivors of childhood cancer are at high risk for experiencing similar symptoms of inattention due to cancer treatment including cranial irradiation and high-dose antimetabolite therapy.<sup>26,27</sup> Recently, the correlation between increased inattention in childhood and later smoking has been evidenced among adults with a childhood history of cancer.<sup>28</sup> The use of stimulant medication (ie, methylphenidate) in reducing inattention among children treated for cancer has primarily examined intervention-related cognitive outcomes in the context of improving academics and social skills. Should further relations be identified between inattention and health behaviors such as smoking in this population, the utility of these pharmacologic interventions could also be tested with regard to prevention/reduction of smoking.

#### *Empiric support for smoking prevention interventions*

Although smoking cessation has been the focus of adult interventions, smoking prevention has been emphasized in adolescent oncology. To our knowledge, there have been 3 interventions targeting smoking outcomes among adolescents with a history of cancer that have utilized randomized experimental designs. Hudson et al.<sup>29</sup> initially reported that a behavioral risk-counseling intervention was unsuccessful in producing significant changes in the areas of health knowledge, perceptions, and a composite of health behaviors (including tobacco use). Yet in a secondary analysis of the data, Cox et al.<sup>30</sup> analyzed the behavioral health outcomes individually and found significant intervention effects. At 12 months' of follow-up, smoking abstinence remained consistent in the treatment group, while decreasing in the control group. Similarly, in a randomized 2-group brief tobacco risk-counseling intervention for adolescent survivors of childhood cancer, Tyc et al.<sup>31</sup> found that those in the intervention group had greater changes in tobacco knowledge, tobacco-related perceived vulnerability, and intentions to smoke compared with those in the control group. Finally, Hollen et al.<sup>7</sup> tested the efficacy of an educational/social support intervention designed to improve decision-making and behavioral risk-taking. Intervention participants significantly improved behavioral health decision-making skills at 1, 6, and 12 months after intervention, and marginally improved smoking behavior at 6 months after intervention. Collectively, these interventions suggest that educational and behavioral risk-counseling interventions are beneficial

in reducing smoking risk among adolescents with a history of cancer up to 12 months after intervention. Long-term follow-up studies are needed to establish whether such interventions are effective in preventing smoking onset and progression to a consistent and/or heavier tobacco use during the high-risk adolescent and young adult years.

#### *Emerging issues in smoking cessation among adolescents with a cancer history*

As noted previously, smoking prevention has been the focus of intervention research among those researchers studying tobacco use in adolescents with a history of cancer, presumably due to the low prevalence of smoking in this population. Yet among the interventions reviewed, 11% to 14% of adolescents self-reported smoking, suggesting that active smoking is a clinically significant problem. Furthermore, this rate of self-reported smoking may be spuriously low due to the perceived consequences associated with smoking disclosure and parent/medical staff reaction. As a result, effective strategies, such as the following emerging areas, are needed to maximize the success of smoking cessation interventions delivered by health care professionals.

**Pharmacotherapy.** In 2000, the Public Health Service Clinical Practice Guidelines for Treating Tobacco Use and Dependence released specific recommendations for tobacco use treatments in children and adolescents.<sup>32</sup> According to one recommendation, clinicians treating adolescents may consider prescriptions for sustained-release bupropion or nicotine replacement therapy (NRT) when there is evidence of nicotine dependence and a desire to quit tobacco use. In addition, because no evidence exists that sustained-release bupropion or NRT is harmful to children and adolescents, these agents may be used when tobacco dependence is obvious. Although it may be premature to recommend the use of pharmacotherapy in treating smoking and nicotine dependence in adolescents with a history of cancer, the following represents a review of the evidence for nicotine replacement therapies and sustained-release bupropion with additional commentary on their use within the context of pediatric cancer.

**Nicotine replacement therapy.** Several studies have examined the efficacy of NRT in reducing smoking among healthy adolescents, with generally mixed findings. Smith et al.<sup>33</sup> examined the efficacy of an 8-week nicotine patch intervention plus individual/group therapy and found that 13.6% of teens had biochemically validated smoking cessation at trial

conclusion, but this fell to 5% at 6-month follow-up. Similar results were obtained in a 6-week nicotine patch therapy plus behavior intervention conducted among 101 smoking adolescents ages of 13 to 17 years.<sup>34</sup> The biologically verified smoking cessation rate was 10.9% after the NRT trial, but only 5% at 6 months of follow-up. Finally, 18% of the adolescent smokers in the study by Hanson et al.<sup>35</sup> did achieve abstinence while utilizing NRT plus cognitive behavioral therapy (CBT) intervention; however, this rate did not differ from the placebo group.

Despite these findings, to our knowledge there is at least 1 well-designed study that found that NRT is effective in reducing smoking among medically at-risk adolescents. Moolchan et al.<sup>36</sup> designed a double-blind, randomized trial that tested the efficacy of 12-week NRT and CBT intervention in achieving biologically verified smoking cessation among 3 groups: nicotine patch (21 mg), nicotine gum (2 mg and 4 mg), and placebo patch or gum. At 17.6%, the 3-month postintervention smoking abstinence rate was highest among teens in the nicotine patch group (compared with 6.5% in the group using gum and 2.5% in the placebo group), with significant differences being identified between the patch and placebo groups.

To our knowledge, no studies to date have reported significant or dangerous side effects related to the use of NRT among healthy adolescents, but NRT has not yet been tested among adolescents with a history of cancer. Contraindications for the use of NRT include serious cardiac arrhythmias, severe or worsening angina, recent myocardial infarction, and hypersensitivity or allergy to nicotine.<sup>37</sup> Although those surviving childhood cancer are not at significantly higher risk than their healthy peers in experiencing these events in adolescence, it is possible that they could experience acute cardiovascular or peripheral vascular disease while receiving treatment. As a result, it is essential that these health issues be considered by prescribing clinicians before the initiation of NRT.

**Burpropion.** To our knowledge, only 2 clinical trials have been published to date examining the efficacy of sustained-release bupropion in adolescents with nicotine dependence. In 2004, Upadhyaya et al.<sup>38</sup> reported the results of an open-label pilot examining the efficacy of sustained-release bupropion plus brief counseling in achieving smoking cessation among 16 adolescents, 11 of whom were diagnosed with ADHD. After a 4-week trial of sustained-release bupropion, the authors reported a biologically verified point prevalence abstinence rate of 31.3%.

Furthermore, the number of cigarettes smoked significantly decreased over the length of the study. Killen et al.<sup>39</sup> conducted a larger clinical trial (N = 211) in which adolescent smokers were randomized to 1 of 2 conditions: nicotine patch plus sustained-release bupropion (at a dose of 150 mg/day) or a nicotine patch plus placebo. Both groups also received group-based skills training. Abstinence rates did not differ significantly between groups; however, the majority of adolescents reduced their daily cigarette consumption with smoking abstinence rates of 23% (patch + sustained-release bupropion) and 28% (patch + placebo) at 10 weeks. To explain these findings, the authors suggested that the dose of sustained-release bupropion was too low compared with the recommended dose of 300 mg/day for adults, and that medication adherence was low.

Contraindications for sustained-release bupropion include known central nervous system (CNS) tumor, current or previous history of seizures, history of bulimia or anorexia nervosa, having used an monoamine oxidase (MAO) inhibitor within the last 2 weeks, and/or abrupt withdrawal from alcohol or tranquilizers.<sup>40</sup> As a result, sustained-release bupropion is not an option for treating nicotine dependence for those adolescents receiving active treatment or those surviving brain or other CNS tumors. Furthermore, the use of this agent must be carefully considered among those patients actively receiving chemotherapy with direct CNS effects due to the increased potential for seizure. Otherwise, there do not appear to be clear contraindications for the use of sustained-release bupropion in the adolescent cancer population, but further research addressing this issue is warranted.

### *Limitations and future directions*

Recent population-based estimates of active smoking among adolescents are reported to be approximately 23%.<sup>4</sup> However, the average rate of tobacco use among active adolescent cancer patients as reported in the literature is 4%, with tobacco use rates ranging from 2% to 14% among adolescents with cancer history.<sup>6,7</sup> These significantly lower rates of tobacco use is surprising given that 20% of adolescents receiving active cancer treatment report past tobacco use, and levels of perceived vulnerability to general health problems and tobacco-related illness are similar to that of their healthy peers.<sup>6</sup> Adolescents differentially disclose engagement in risky behaviors based on the setting of disclosure, with perceived anonymity impacting the validity of the behavioral report.<sup>41</sup> Kann et al.<sup>42</sup> found that the behavioral prevalence estimates, which were primarily affected by setting

among adolescents, were health behaviors that are illegal (eg, smoking for those age younger than 18 years) or socially stigmatized. These findings, along with the social benefits of underreporting smoking within a cancer context, question the validity of self-reported tobacco use among adolescents with a history of cancer. It is essential that future studies be conducted in which the validity of self-reported smoking (compared with biologic measures of smoking) is established in this high-risk population.

The optimal timing for implementing tobacco risk education in pediatric cancer patients necessitates further research. Unlike with adult oncology patients, the delivery of these interventions to pediatric patients at or soon after diagnosis may preclude receptivity to smoking-related interventions (unpublished data). Studies need to elucidate whether adolescent patients may be more amenable to receiving health risk counseling early during treatment and diagnosis. Furthermore, the treatment context for adolescent oncology is ripe for addressing tobacco issues within the patient's family. Parents are often distressed at the time of their child's cancer diagnosis and smoking cessation efforts may not be appropriate at this time. Yet parent-delivered interventions designed to reduce the patient's secondhand smoke exposure may be an appropriate alternative. This way the family could assist in reducing their child's risk of tobacco-related disease while increasing their self-efficacy related to changing their tobacco behaviors.

Establishing predictive models of smoking initiation among nonsmoking adolescent cancer patients is also critically important to the development of effective smoking prevention interventions. To our knowledge, there have been 3 smoking prevention trials to date conducted among adolescent survivors that have positively affected smoking-related risk factors. However, none of these studies included follow-up periods beyond 12 months after intervention. Long-term studies are needed to demonstrate the utility of these established interventions in preventing smoking as these teens progress through their high-risk smoking years. Preadolescent and early-adolescent studies examining the predictive validity of intentions to smoke (as it relates to later smoking) would also be beneficial. Should this relation be established in adolescents with a history of cancer, much as it has in healthy adolescents, interventions could target nonsmoking patients who waver in their commitment to remaining tobacco free.

The use of pharmacotherapy in treating young nicotine-dependent patients should also be the focus of future research. There is preliminary support in demonstrating the safety of NRT and sustained-

release bupropion, and limited support for these therapies in reducing tobacco use among healthy adolescents. There also appears to be particular promise in the use of these methods in reducing smoking among adolescents with attention deficit hyperactivity disorder. As a result, these interventions may be particularly useful for pediatric patients experiencing inattention and/or slowed processing speed, 2 common cognitive late effects experienced by those treated for childhood cancer. Once the safety of these products is established, researchers may also examine the utility of other NRTs (ie, gum, lozenges, and inhalers) that may assist in reducing the lack of adherence often cited in these studies.

### **Adults Receiving Treatment and Surviving Cancer** ***Smoking prevalence***

Several large studies have been conducted to establish the prevalence of tobacco use in adult cancer patients. In 2003, Samant and Tucker<sup>43</sup> reviewed the medical records of 15,850 adult cancer patients and found that 26% of men and 23% of women were current smokers after cancer treatment. These patients smoked approximately 1 pack per day, with men smoking more than women. In the largest study of 25,436 cancer patients, 56% of patients reported having a smoking history, with 5-year survival rates being 55.4% and 43.5% for nonsmokers and smokers, respectively.<sup>44</sup> In contrast, only 17% of adult survivors of childhood cancer report current smoking.<sup>45</sup>

### ***Adverse health outcomes associated with tobacco use***

Cancer patients who smoke are at extremely high risk for tobacco-related morbidity and mortality not only due to the carcinogenic effects of smoking but to the side effects of cancer treatment as well. Head and neck patients who continue to smoke after a diagnosis of cancer, for example, experience an increased rate and duration of symptoms,<sup>46</sup> diminished efficacy of RT,<sup>47</sup> reduced survival time,<sup>48</sup> and a greater risk of disease recurrence or a second primary tumor.<sup>49</sup> The adverse effects of smoking may also impede treatment-related recovery. For example, Goodwin et al.<sup>50</sup> found that overall complications, reconstructive failure, mastectomy flap necrosis, and infectious complications were higher in smokers undergoing postmastectomy reconstruction than nonsmokers. Cigarette smoking and RT have a multiplicative effect on the risk of subsequent lung cancer in survivors of Hodgkin disease.<sup>51</sup> Among adult survivors of childhood cancer who smoke, for example, those who received alkylating agents are at higher

risk for pulmonary fibrosis,<sup>52</sup> urinary tract toxicity,<sup>53</sup> and bladder malignancy<sup>54</sup> compared with nonsmoking cancer patients.

### ***Benefits associated with smoking cessation*** ***postcancer diagnosis***

Smoking cessation results in multiple health benefits among those diagnosed with cancer. Primary benefits include increased survival rates, decreased subsequent malignancies, and reduced medical complications. Among patients with nonsmall cell lung cancer patients, a longer duration of smoking abstinence after diagnosis was associated with a lower risk of mortality among females.<sup>55</sup> Smoking cessation has also been associated with reduced toxicity and increased respiratory functioning, 2 health features that are associated with positive health outcomes in cancer patients.<sup>56,57</sup> The recent literature indicates that continued smoking after cancer treatment is also associated with significant reductions in quality of life in physical, cognitive, and social domains.<sup>58</sup> Patients who abstained from smoking after treatment of oral/oropharyngeal malignancy, for example, experienced decreased depression and anxiety compared with continued smokers.<sup>59</sup> Overall, the evidence suggests that smoking cessation after a diagnosis of cancer is beneficial in terms of increased survival and quality of life, and decreased subsequent malignancy and psychologic distress.

### ***Factors associated with continued tobacco use*** ***or cessation postcancer diagnosis***

Although we have not yet established well-developed models that predict smoking behavior after the diagnosis of cancer, specific demographic, medical, and psychologic/behavioral variables have been implicated. Being male, younger age, lower educational level, and smoking among family/social network members appear to place one at smoking risk.<sup>60–62</sup> Medically speaking, continued smokers are less likely to have extensive disease, oral cavity disease, or postoperative treatment with RT<sup>63</sup> and more likely to have completed cancer treatment.<sup>61</sup> Psychologic factors such as lower levels of perceived health risk, quitting self-efficacy and tobacco knowledge, higher levels of self-reported quitting cons, fatalistic beliefs, and alcohol use have all been associated with continued smoking among adults with a cancer history.<sup>62,64–66</sup>

Although tobacco use after cancer diagnosis remains a clinically significant problem, research suggests that many of these continued smokers desire to quit. Ostroff et al.<sup>63</sup> found that 93% of continuous smoking patients treated for bladder carcinoma were contemplating or preparing to stop

smoking. Male survivors, those diagnosed at older age, those who had a higher perceived vulnerability for smoking-related illness, and those with increased social support to quit were more confident in their ability to quit and more ready to change their smoking behaviors.<sup>67,68</sup> These findings are encouraging in that higher patient motivation (or 'readiness') to stop smoking appears to predict smoking cessation in these continued smoking patients. Medically, more extensive disease, tumor site, increased severity of toxicity, and increased physical barriers to continued smoking have all been associated with smoking cessation.<sup>68-71</sup> Patients diagnosed at later cancer stages appear to be nearly 3 times more likely to be continuous abstainers compared with those with earlier staged disease.<sup>65</sup> The number of quit attempts before and after diagnosis and counsel at the time of diagnosis have also been associated with higher rates of smoking cessation among continued smokers.<sup>66,69</sup>

#### ***Emerging issues in smoking cessation among adults with a cancer history***

Despite being the non-NRT agent of choice in 100% of the oncology smoking cessation trials, the use of bupropion is contraindicated among those with a history of CNS tumors due to an increased risk of seizures, thereby limiting its usefulness in adult oncology populations. As a result, additional smoking cessation options need to be explored for these high-risk patients. Nicotine vaccine and varenicline are 2 emerging treatments for smoking that may prove to be useful for adult oncology patients in the future.

**Nicotine vaccine.** NicVAX (Nabi, Boca Raton, Fla), TA-NIC (Xenova, Berkshire, UK), and Nicotine-Qbeta (Cytos, Zurich, Switzerland) are examples of nicotine vaccines currently under development. Although these vaccines are not yet approved by the U. S. Food and Drug Administration (FDA), preliminary data from phase 1 and phase 2 trials examining the efficacy and safety of the nicotine vaccine appear promising.<sup>70,71</sup> These vaccines differ from traditional pharmacologic therapies in that the body's immune system is utilized to produce antibodies that effectively block nicotine from crossing the blood-brain barrier. The resulting reduction in nicotine-related reinforcing effects is proposed to lead to smoking extinction. Because the nicotine vaccine does not interact directly with the brain, smoking patients with CNS tumors may not be at increased risk of experiencing adverse side effects such as seizures. Further studies examining the safety and utility of nicotine vaccines in both adults with and without cancer are warranted.

**Varenicline.** Although all smoking cessation trials conducted with adult oncology patients have examined the usefulness of bupropion, emerging research suggests that varenicline is more effective in achieving smoking cessation. Varenicline (Chantix; Pfizer, New York, NY), a recently FDA-approved smoking cessation aid, is a selective nicotine receptor partial agonist designed to reduce nicotine-related withdrawal and craving while concurrently blocking the reinforcing effects of nicotine.<sup>72</sup> Among 3 randomized controlled clinical trials, varenicline was found to be significantly more effective than bupropion at achieving both short-term and long-term carbon monoxide-confirmed smoking cessation rates.<sup>73-75</sup> Furthermore, there are no known contraindications associated with varenicline, although it is not recommended for those who are pregnant, nursing, or age younger than 18 years.<sup>76,77</sup> This suggests that, unlike bupropion, this drug is more appropriate for adults with a history of CNS tumor and seizure, and may have better overall safety and generalizability to the cancer population.

#### ***Empirically supported interventions for smoking cessation by discipline***

**Medical providers.** To our knowledge few studies conducted over the past 10 years have utilized a randomized or matched case-control design to evaluate the effectiveness of smoking interventions among patients with cancer. Regarding the efficacy of a nurse-based minimal contact smoking intervention, Griebel et al.<sup>78</sup> did not find significant differences in abstinence rates between those in usual care and those who were part of intervention groups. Similarly, Schnoll et al.<sup>79</sup> also did not identify significant differences among patients assigned to either a National Institutes of Health physician-based brief intervention or usual care. It is interesting to note that the authors found increased levels of quit motivation among those with tobacco-related illnesses, with lung or head/neck cancer patients having comparatively higher smoking cessation rates at both 6 months and 12 months. These findings suggest that oncology patients with tobacco-related cancers may have the best smoking cessation outcomes due, at least in part, to increased quit motivation. Duffy et al.<sup>80</sup> assessed the efficacy of a nurse-based CBT intervention for smoking cessation among patients with head and neck cancer. At the 6-month follow-up, 47% of the intervention participants reported smoking cessation compared with 31% in the usual care group. Cessation rates continued to be significantly higher among smokers with comorbid alcohol problems and/or depression in the intervention group

**TABLE 1**  
**Recommendations for Clinicians in the Assessment and Intervention of Tobacco Use Among Adolescents and Their Families With a Cancer History**

| Directives                  | Steps                                                                                                                                                                                                                                                                                                                                                                                |
|-----------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ASK about tobacco use       | 1. If current past tobacco use is denied, ask about future intentions concerning tobacco use.                                                                                                                                                                                                                                                                                        |
| ADVISE                      | 2. Also ask about the tobacco use among family members or others living in the home, and secondhand smoke exposure.<br>1. Provide a clear, strong, and personalized message of total tobacco abstinence to pediatric cancer patients and their families.<br>2. Discuss the patient's heightened vulnerability to tobacco-related disease as a survivor of childhood cancer.          |
| ASSESS                      | 3. Individualize messages specific to the patient's treatment history, current clinical condition, and organs most vulnerable to treatment, along with the possibility of second cancers as it relates to tobacco use.<br>1. Determine if the patient and other tobacco users in the family are willing to make a quit attempt.                                                      |
| ASSIST in tobacco cessation | 2. If the patient or family member is willing to make a quit attempt, provide developmentally appropriate tobacco cessation counseling.<br>1. Clinicians should prepare adolescents to quit their tobacco use while considering a referral to a community-, school-, or hospital-based intervention program.                                                                         |
| ARRANGE                     | 2. Consider pharmacotherapy for adolescents 18 years of age and older. NOTE: Clinicians should be confident of the patient's tobacco dependence, intention to quit, and health status as it relates to agent contradictions prior to instituting the use of pharmacotherapy.<br>1. Schedule a follow-up contact in person or by telephone within the first week after the quit date. |

Adapted from: Fiore MC, Bailey WC, Cohen, SJ, et al. Treating Tobacco Use and Dependence. Quick Reference Guide for Clinicians. Rockville, MD: U.S. Department of Health and Human Services, Public Health Service; 2000.

than among those in usual care, highlighting the utility of holistically treating comorbid presentations as opposed to treating each problem independently.<sup>80</sup>

*Peer-delivered.* Emmons et al.<sup>81</sup> and Park et al.<sup>82</sup> evaluated the efficacy of a peer-based smoking cessation intervention delivered to adult survivors of childhood cancer. Smokers were randomly assigned to receive a telephone-based motivational intervention, and NRT if indicated. At 8 months, 14.5% of the participants quit smoking, with smoking cessation rates being higher among those in the intervention group. Similar results were found at the 12-month follow-up.<sup>81</sup> The study by Park et al.<sup>82</sup> focused on the differences between the participants in the intervention group and found that smoking cessation rates improved to 20% among those who received 5 to 6 telephone calls. Of the participants who received NRT, 36% made at least 1 quit attempt compared with 26% of those who did not, suggesting that NRT is a useful adjunctive to smoking cessation interventions in cancer populations.

*Mental health associates.* Cox et al.<sup>68</sup> examined the effectiveness of a nicotine dependence intervention among patients diagnosed with and those without lung cancer. The 7-day point prevalence tobacco abstinence rates at 6 months were 22% for patients diagnosed with lung cancer and 14% for matched controls. The results were no longer statistically significant after adjusting for age, sex, mean number of cigarettes smoked per day 6 months before intervention, and stage of change. Despite this, there was evidence supporting the utility of early cessation

treatment efforts after a diagnosis of lung cancer. Similarly, Garces et al.<sup>83</sup> found that smoking cessation in head/neck cancer patients was significantly associated with shorter time between cancer diagnosis and intervention, suggesting that adults newly diagnosed with cancer may be more receptive to cessation efforts.

### Limitations and Future Directions

Findings from studies investigating smoking behaviors of cancer patients should be interpreted in the context of their limitations. Several studies reviewed rely on the patient's self-report of smoking, which may underestimate actual smoking prevalence.<sup>41</sup> Furthermore, some studies used archival data from medical records that may not discriminate between onset of tobacco use, smoking status during treatment, and smoking status after treatment. Therefore, it is difficult to pinpoint both onset and possible cessation of tobacco use throughout the course of treatment.<sup>84</sup> Many of the studies in the literature have also been conducted with relatively small sample sizes, limited ethnic diversity, referral bias, and lack of control groups, which can undermine their internal validity and adversely affect generalizability. Finally, interventions for cancer patients may need to be tailored to the person's level of readiness to quit and incorporate a familial social support component to enhance treatment outcomes.<sup>85</sup>

As this article suggests, smoking cessation interventions as delivered to adult cancer patients are frequently ineffective and have been generally understudied. In addition to improving the aforementioned

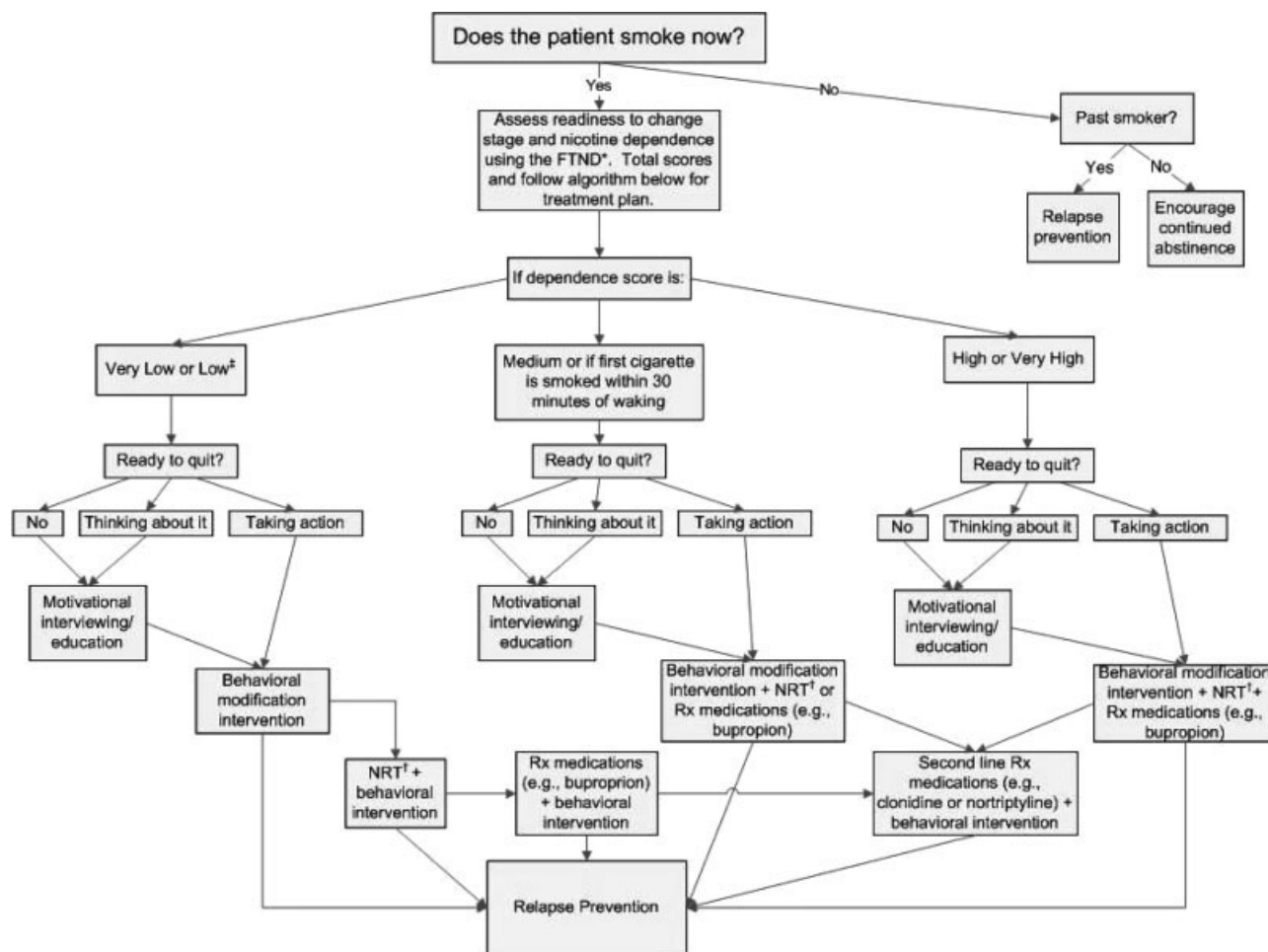


**FIGURE 1.** Stop-smoking algorithms for patients with cancer. Adapted from Fiore et al.<sup>2</sup> \*FTND indicates Fagerstrom test for nicotine dependence. <sup>†</sup>NRT indicates nicotine replacement therapy. <sup>‡</sup>Only in rare cases will low nicotine-dependent, ready-to-quit smokers have to resort to nicotine replacement therapy or prescription (Rx) medications for smoking cessation.

methodologic limitations, future cessation trials should examine the efficacy of pharmacotherapies due to their demonstrated efficacy at increasing smoking cessation among healthy populations. Furthermore, tailored interventions taking into account sex, race, readiness to quit, and individual differences such as disease site, disease type, stage of disease, and treatment need to be tested.<sup>86</sup> Once smoking cessation is achieved, additional research is needed to examine the factors predictive of lapse so that appropriate relapse prevention interventions can be developed. Further identification of the benefits of smoking cessation will assist clinicians as they develop persuasive arguments as to why the cancer patient should quit smoking. Finally, research addressing the context (ie, inpatient vs outpatient setting, individual vs familial) and method of presentation of risk information (eg, health care provider vs peer, group vs individual, computer vs provider-delivered,

telephone quit line vs smoking literature) is also warranted to identify the most effective mechanism for the delivery of antismoking messages. In this regard, particular interest has developed in smoking cessation programs that involve families of cancer patients. Specific issues that should be examined include the role of the family in supporting smoking cessation in cancer patients, how a diagnosis of cancer affects familial smoking behavior, and whether family-based smoking interventions would be beneficial. Finally, examination of interventions that address patient exposure to secondary tobacco smoke would provide a comprehensive approach to tobacco control in this population.

### Recommendations for Clinician-Delivered Tobacco Counseling

It is crucial that healthcare providers involved in the diagnosis, treatment, and/or long-term care of cancer patients take a primary role in counseling patients

regarding the dangers of tobacco use and encourage tobacco abstinence because brief physician-delivered counseling has a documented beneficial impact on smoking behaviors.<sup>87</sup> However, healthcare providers do not routinely engage in tobacco control screening and counseling<sup>88</sup> due to time constraints, lack of compensation by third-party payers for smoking cessation counseling, and limited training in how to deliver antitobacco messages. At a minimum, practice guidelines<sup>32</sup> suggest that healthcare providers should routinely incorporate the “5 A’s” into the patient’s routine medical care, as implementation of the Public Health Service recommendations has been shown to double smoking cessation rates compared with those in standard care conditions.<sup>85</sup> Table 1 contains directives that are based on the Public Health Service recommendations but are adapted for use in assessing and intervening in tobacco use among adolescents with a history of cancer and their families. The algorithm in Figure 1 was developed to provide clinicians with an aid to promote smoking cessation among adult cancer patients. This algorithm was adapted from Fiore et al.’s<sup>2</sup> “screen for tobacco use status” to better fit the needs of cancer patients in a clinical environment.

## Conclusions

As outlined in this review, 2% to 26% of adolescents and adults receiving treatment and surviving cancer are engaged in smoking behaviors. That these behaviors are occurring despite the existence of heightened health risks associated with tobacco use within the context of cancer treatment is of significant importance. As such, research targeting smoking issues among those with a cancer history is critical to address the assessment, prevention, and intervention limitations that currently exist in this population. Furthermore, emerging treatments, such as sustained-release bupropion for adolescents and varenicline for adults, warrant consideration, as do the contributions of genotyping and psychologic distress in smoking onset and maintenance. Together, these considerations may one day yield the development of the efficacious prevention and smoking cessation programs needed in this high-risk population.

## REFERENCES

- Centers for Disease Control and Prevention: annual smoking-attributable mortality, years of potential life lost, and economic costs—United States 1995–1999. *MMWR Morb Mortal Wkly Rep.* 2004;51:300–303.
- Fiore M, Bailey WC, Cohen SJ. Treating tobacco use and dependence. Clinical Practice Guideline. Rockville, MD: U.S. Department of Health and Human Services; 2000.
- Ries LAG, Eisner MP, Kosary CL, et al. Cancer statistics review, 1973–1999. Bethesda, MD: National Cancer Institute; 2002.
- Allen JA, Vallone D, Haviland ML, et al. Tobacco use among middle and high school students. *MMWR Morb Mortal Wkly Rep.* 2003;52:1096–1098.
- Mulhern RK, Tyc VL, Phipps S, et al. Health-related behaviors of survivors of childhood cancer. *Med Pediatr Oncol.* 1995;25:159–165.
- Tyc VL, Lensing S, Klosky J, Rai SN. A comparison of tobacco-related risk factors between adolescents with and without cancer. *J Pediatr Psychol.* 2004;30:359–370.
- Hollen PJ, Hobbie WL, Finley SM. Testing the effects of a decision-making and risk-reduction program for cancer-surviving adolescents. *Oncol Nurs Forum.* 1999;26:1475–1486.
- U.S. Department of Health and Human Services. Preventing tobacco use among young people: a report of the Surgeon General. Atlanta, GA: 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; 1994.
- Arday DR, Giovino GA, Schulman J, Nelson DE, Mowery P, Samet JM. Cigarette smoking and self-reported health problems among US high school seniors, 1982–1989. *Am J Health Promot.* 1995;10:111–116.
- Hak DJ, Lee SS, Goulet JA. Success of exchange reamed intramedullary nailing for femoral shaft nonunion or delayed union. *J Orthop Trauma.* 2000;14:178–182.
- Children’s Oncology Group. Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers. Available at URL: <http://www.survivorshipguidelines.org> Accessed on February 2, 2007.
- O’Driscoll BR, Hasleton PS, Taylor PM, Poulter LW, Gattamaneni HR, Woodcock AH. Active lung fibrosis up to 17 years after chemotherapy with carmustine (BCNU) in childhood. *N Engl J Med.* 1990;323:378–382.
- Benoist MR, Lemerle J, Jean R. Effects on pulmonary function of whole lung irradiation for Wilm’s tumor in children. *Thorax.* 1982;37:175–180.
- Lipshultz SE, Colan SD, Gelbar RD, Perez-Atayde AR, Sallan SE, Sanders SP. Late cardiac effects of doxorubicin therapy for acute lymphoblastic leukemia in childhood. *N Engl J Med.* 1991;324:808–815.
- Kaste SC, Rai SN, Fleming K, et al. Changes in bone mineral density in survivors of childhood acute lymphoblastic leukemia. *Pediatr Blood Cancer.* 2006;46:77–87.
- Tyc VL, Hadley W, Crockett G. Brief report: predictors of intentions to use tobacco among adolescent survivors of cancer. *J Pediatr Psychol.* 2001;26:117–121.
- Robinson LA, Klesges RC, Zbikowski SM, Glaser R. Predictors of risk for different stages of adolescent smoking in a biracial sample. *J Consult Clin Psychol.* 1997;65:653–662.
- Lerman C, Audrain J, Main D, et al. Evidence suggesting the role of specific genetic factors in cigarette smoking. *Health Psychol.* 1999;18:14–20.
- Comings D, Ferry L, Bradshaw-Robinson S, Burchette R, Chiu C, Muhleman D. The dopamine D2 receptor (DRD2) gene: a genetic risk factor in smoking. *Pharmacogenetics.* 1996;6:73–79.
- Spitz M, Shi H, Yang F, Hudmon K, Jiang H, Chamberlain R. Case-control study of the D2 dopamine receptor gene and smoking status in lung cancer patients. *J Natl Cancer Inst.* 1998;90:358–363.

21. Tercyak KP, Nicolas M, Councill T, Prahlad S, Taylor KL, Shad AT. Brief report: health beliefs among survivors of childhood cancer. *J Pediatr Psychol*. 2004;29:397-402.
22. Audrain-McGovern J, Lerman C, Wileyto EP, Rodgiques D, Shields PG. Interacting effects of genetic predisposition and depression on adolescent smoking progression. *Am J Psychiatry*. 2004;161:1224-1230.
23. Leventhal H, Cleary PD. The smoking problem: a review of the research and theory in behavioral risk modification. *Psychol Bull*. 1980;88:370-405.
24. Hobbie WL, Stuber M, Meeske K, et al. Symptoms of post-traumatic stress in young adult survivors of childhood cancer. *J Clin Oncol*. 2000;18:4060-4066.
25. Upadhyaya HP, Rose K, Wang W, et al. Attention-deficit/hyperactivity disorder, medication treatment, and substance use patterns among adolescents and young adults. *J Child Adolesc Psychopharmacol*. 2005;15:799-809.
26. Reddick WE, Shan ZY, Glass JO, et al. Smaller white-matter volumes are associated with larger deficits in attention and learning among long-term survivors of acute lymphoblastic leukemia. *Cancer*. 2006;106:941-949.
27. Reeves CB, Palmer SL, Reddick WE, et al. Attention and memory functioning among pediatric patients with medulloblastoma. *J Pediatr Psychol*. 2006;31:272-280.
28. Schum LN, Robinson LA, Tyc VL, Hinds PS, Hudson MM, Robison LL. Attention problems as a risk factor for smoking among survivors of childhood cancer. Poster presented at Psychosocial and Neurocognitive Consequences of Childhood Cancer: A Symposium in Tribute to Raymond K. Mulhern; Memphis, TN. September 13-15, 2006.
29. Hudson MM, Tyc VL, Srivastava DK, et al. Multi-component behavioral interventions to promote health protective behaviors in childhood cancer survivors: the Protect Study. *Med Pediatr Oncol*. 2002;39:2-11.
30. Cox CL, McLaughlin RA, Rai SN, Steen BD, Hudson MM. Adolescent survivors: a secondary analysis of a clinical trial targeting behavior change. *Pediatr Blood Cancer*. 2005;45:144-154.
31. Tyc VL, Rai S, Lensing S, Klosky J, Stewart D, Gattuso J. Intervention to reduce intentions to use tobacco among pediatric cancer survivors. *J Clin Oncol*. 2003;21:1366-1372.
32. Fiore MC, Bailey WC, Cohen SJ, et al. Treating tobacco use and dependence. Quick reference guide for clinicians. Rockville, MD: U.S. Department of Health and Human Services, Public Health Service; 2000.
33. Smith T, House R, Croghan I, et al. Nicotine patch therapy in adolescent smokers. *Pediatrics*. 1996;98:659-667.
34. Hurt R, Croghan G, Beede S, Wolter T, Croghan I, Patten C. Nicotine patch therapy in 101 adolescent smokers. *Arch Pediatr Adolesc Med*. 2000;154:31-37.
35. Hanson K, Allen S, Hatsukami D. Treatment of adolescent smokers with the nicotine patch. *Nicotine Tob Res*. 2003;5:515-526.
36. Moolchan E, Robinson M, Ernst M, et al. Safety and efficacy of the nicotine patch and gum for the treatment of adolescent tobacco addiction. *Pediatrics*. 2005;115:407-414.
37. Fiore M, Bailey WC, Cohen SJ, et al. Treating tobacco use and dependence. In: Clinical Practice Guideline. Rockville, MD: U.S. Department of Health and Human Services; 2000.
38. Upadhyaya HP, Brady KT, Wang W. Bupropion SR in adolescents with comorbid ADHD and nicotine dependence: a pilot study. *J Am Acad Child Adolesc Psychiatry*. 2004;43:199-205.
39. Killen JD, Robinson TN, Ammerman S, et al. Randomized clinical trial of the efficacy of bupropion combined with nicotine patch in the treatment of adolescent smokers. *J Consult Clin Psychol*. 2004;72:729-735.
40. Zyban. Prescribing information. Available at URL: [http://us.gsk.com/products/assets/us\\_zyban.pdf](http://us.gsk.com/products/assets/us_zyban.pdf) Accessed on February 1, 2007.
41. Weinstein ND. Testing 4 competing theories of health-protective behavior. *Health Psychol*. 1993;12:324-333.
42. Kann L, Brener ND, Warren CW, Collins JL, Giovino GA. An assessment of the effect of data collection setting on the prevalence of health risk behaviors among adolescents. *J Adolesc Health*. 2002;31:327-335.
43. Samant R, Tucker T. Analysis of cigarette smoking habits of cancer patients referred to the Northeastern Ontario Regional Cancer Centre. *J Cancer Educ*. 2003;18:157-160.
44. Yu GP, Ostroff JS, Zhang ZF, Tang J, Schantz SP. Smoking history and cancer patient survival: a hospital cancer registry study. *Cancer Detect Prev*. 1997;21:497-509.
45. Emmons K, Li FP, Whitton J, et al. Predictors of smoking initiation and cessation among childhood cancer survivors: a report from the Childhood Cancer Survivor Study. *J Clin Oncol*. 2002;20:1608-1616.
46. Des Rochers C, Dische S, Sanders MI. The problem of cigarette smoking in radiotherapy for cancer in the head and neck. *Clin Oncol*. 1992;4:214-216.
47. Cinciripini PM, Gritz ER, Tsoh JY, Skaar KL. Smoking cessation and cancer prevention. In: Holland JC, editor. *Psycho-Oncology*. New York: Oxford University Press; 1998.
48. Goodman MT, Kolonel LN, Wilkens LR, Yoshizawa CN, Le Marchand L. Smoking history and survival among lung cancer patients. *Cancer Causes Control*. 2005;1:155-163.
49. Day GL, Blot WJ, Shore RE, et al. Second cancers following oral and pharyngeal cancers: role of tobacco and alcohol. *J Natl Cancer Inst*. 1994;86:131-137.
50. Goodwin SJ, McCarthy CM, Pusic AL, et al. Complications in smokers after postmastectomy tissue expander/implant breast reconstruction. *Ann Plast Surg*. 2005;55:16-19.
51. Boivin J. Smoking, treatment for Hodgkin's disease, and subsequent lung cancer risk. *J Natl Cancer Inst*. 1995;87:1502-1503.
52. Muller J. Disturbance of pubertal development after cancer treatment. *Best Pract Res Clin Endocrinol Metab*. 2002;16:91-103.
53. Heyn R, Raney B, Hays D, et al. Late effects of therapy in patients with paratesticular rhabdomyosarcoma. *J Clin Oncol*. 1992;10:614-623.
54. Kersun L, Wimmer R, Hoot A, Meadows A. Secondary malignant neoplasms of the bladder after cyclophosphamide treatment of childhood acute lymphocytic leukemia. *Pediatric Blood Cancer*. 2004;42:289-291.
55. Ebbert JO, Williams BA, Sun Z, et al. Duration of smoking abstinence as a predictor for non small lung cancer survival in women. *Lung Cancer*. 2005;47:165-172.
56. Okubo K, Mark EJ, Flieder D, et al. Bronchoalveolar carcinoma: clinical, radiologic, and pathologic factors and survival. *J Thorac Cardiovasc Surg*. 1999;118:702-709.
57. Sanderson Cox L, Sloan JA, Patten CA, et al. Smoking behavior of 226 patients with diagnosis of stage IIIA/IIIB non-small cell lung cancer. *Psychooncology*. 2002;11:472-478.
58. 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 Oncol*. 2007;43:187-192.

59. Humphris GM, Rogers SN. The association of cigarette smoking and anxiety, depression and fears of recurrence in patients following treatment of oral and oropharyngeal malignancy. *Eur J Cancer Care*. 2004;13:328–335.
60. Emmons K, Butterfield R, Puleo E, et al. Smoking among participants in the childhood cancer survivors cohort: the partnership for health study. *J Clin Oncol*. 2003;21:189–196.
61. Schnoll RA, Malstrom M, James C, et al. Correlates of tobacco use among smokers and recent quitters diagnosed with cancer. *Patient Educ Couns*. 2002;46:137–145.
62. Schnoll RA, Engstrom PF, Subramanian S, Demidov L, Wielt DB, Tighiouart M. Prevalence and correlates of tobacco use among Russian cancer patients: implications for the development of smoking cessation interventions at a cancer center in Russia. *Int J Behav Med*. 2006;13:16–25.
63. Ostroff J, Garland J, Moadel A, et al. Cigarette smoking patterns in patients after treatment of bladder cancer. *J Cancer Educ*. 2000;15:86–90.
64. Schnoll RA, James C, Malstrom M, et al. Longitudinal predictors of continued tobacco use among patients diagnosed with cancer. *Ann Behav Med*. 2003;25:214–221.
65. Lambert MT, Terrell JE, Copeland LA, Ronis DL, Duffy SA. Cigarettes, alcohol, and depression: characterizing head and neck cancer survivors in 2 systems of care. *Nicotine Tob Res*. 2005;7:233–241.
66. Ark WV, DiNardo LJ, Oliver DS. Factors affecting smoking cessation in patients with head and neck cancer. *Laryngoscope*. 1997;107:888–892.
67. Gritz ER, Carr CR, Rapkin D, et al. Predictors of long-term smoking cessation in head and neck cancer patients. *Cancer Epidemiol Biomarkers Prev*. 1993;2:261–270.
68. Cox LS, Patten CA, Ebbert JO, et al. Tobacco use outcomes among patients with lung cancer treated for nicotine dependence. *J Clin Oncol*. 2002;20:3461–3469, 2002.
69. Chan Y, Irish JC, Wood SJ, et al. Smoking cessation in patients diagnosed with head and neck cancer. *J Otolaryngol*. 2004;33:75–81.
70. Hatsukami DK, Rennard S, Jorenby D, et al. Safety and immunogenicity of a nicotine conjugate vaccine in current smokers. *Clin Pharmacol Ther*. 2005;78:456–467.
71. Cornuz J, Klinger K, Mueller P, et al. A therapeutic vaccine for nicotine dependence: results of a phase I and a randomized phase II study. Presented at: American Society of Clinical Oncology, Orlando, Florida, May 13–17, 2005.
72. Cahill K, Stead LE, Lancaster T. Nicotine receptor partial agonists for smoking cessation. *Cochrane Database Syst Rev* 2007;1:CD006103.
73. Gonzales D, Rennard SI, Nides M, et al. Varenicline, an alpha4beta2 nicotinic acetylcholine receptor partial agonist, vs sustained-release bupropion and placebo for smoking cessation: a randomized controlled trial. *JAMA*. 2006;296:47–55.
74. Nides M, Oncken C, Gonzales D, et al. Smoking cessation with varenicline, a selective alpha4beta2 nicotinic receptor partial agonist: results from a 7-week, randomized, placebo- and bupropion-controlled trial with 1-year follow-up. *Arch Intern Med*. 2006;166:1561–1568.
75. Jorenby DE, Hays JT, Rigotti NA, et al. Efficacy of varenicline, an alpha4beta2 nicotinic acetylcholine receptor partial agonist, vs placebo or sustained-release bupropion for smoking cessation: a randomized controlled trial. *JAMA*. 2006;296:56–63.
76. Pfizer Laboratories. Chantix (varenicline) tablets prescribing information. New York: Pfizer; 2006.
77. Pfizer for Professionals. Chantix tablets: indications and usage. Available at URL: [https://www.pfizerpro.com/product\\_info/chantix\\_pi\\_indications\\_and\\_usage.jsp](https://www.pfizerpro.com/product_info/chantix_pi_indications_and_usage.jsp) Accessed February 10, 2007.
78. Griebel B, Wewers ME, Baker CA. The effectiveness of a nurse-managed minimal smoking-cessation intervention among hospitalized patients with cancer. *Oncol Nurs Forum*. 1998;25:897–902.
79. Schnoll RA, Zhang B, Montsettar R, et al. Brief physician-initiated quit smoking strategies for clinical oncology settings: a trial coordinated by the Eastern Cooperative Oncology Group. *J Clin Oncol*. 2003;21:355–365.
80. Duffy SA, Ronis DL, Valenstein M, et al. A tailored smoking, alcohol, and depression intervention for head and neck cancer patients. *Cancer Epidemiol Biomarkers Prev*. 2006;15:2203–2208.
81. Emmons KM, Puleo E, Park E, et al. Peer-delivered smoking counseling for childhood cancer survivors increases rate of cessation: the partnership for health study. *J Clin Oncol*. 2005;23:6516–6523.
82. Park ER, Puleo E, Butterfield RM, et al. A process evaluation of a telephone-based peer-delivered smoking cessation intervention for adult survivors of childhood cancer: the partnership for health study. *Prev Med*. 2006;42:435–442.
83. Garces YI, Schroeder DR, Nirelli LM, et al. Tobacco use outcomes among patients with head and neck carcinoma treated for nicotine dependence: a matched-pair analysis. *Cancer*. 2004;101:116–124.
84. Tyas SL, Pederson LL. Psychosocial factors related to adolescent smoking: a critical review of the literature. *Tob Control*. 1998;7:409–420.
85. Katz DA, Muehlenbruch DR, Brown RB, Fiore MC, Baker TB, for the AHRQ Smoking Cessation Guideline Study Group. Effectiveness of a clinic-based strategy for implementing the AHRQ smoking cessation guideline in primary care. *Prev Med*. 2002;35:293–301.
86. Mackie E, Hill J, Kondryn H, McNally R. Adult psychosocial outcomes in long-term survivors of acute lymphoblastic leukaemia and Wilms' tumour: a controlled study. *Lancet*. 2000;355:1310–1314.
87. Fiore MC, Bailey WC, Cohen SE. Smoking cessation. Clinical Practice Guideline No. 18. Washington, DC: Department of Health and Human Services, Public Health Service, Agency for Health Care Policy and Research, and Centers for Disease Control; 1996.
88. Frankowski BL, Weaver SO, Secker-Walker RH. Advising parents to stop smoking: pediatricians' and parents' attitudes. *Pediatrics*. 1993;91:296–300.