

# Health Behaviors Influence Cancer Survival

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In this issue of *Journal of Clinical Oncology*, Duffy et al<sup>1</sup> have provided important evidence of the effect of pretreatment health behaviors on all-cause survival in a prospective cohort study of patients enrolled in the University of Michigan Head and Neck Cancer Specialized Program of Research Excellence (SPORE; Ann Arbor, MI). Analyses of data from 504 participants showed that smoking status (current or former) was the strongest predictor of survival in both univariate and multivariate analyses. In the univariate analysis only, problem drinking, low fruit intake and low level of physical activity negatively affected survival. Low vegetable intake and poor sleep behavior were not significant in either analysis. We comment on the importance of these findings and offer suggestions for additional research, concentrating primarily on smoking behavior, alcohol, diet, and physical activity.

## TOBACCO USE

There is extensive documentation of the prognostic impact of smoking behavior on second primary tumors, recurrence, and survival in head and neck cancer. Adverse impacts on cancer treatment effectiveness and complications,<sup>2-5</sup> additional disease,<sup>6-8</sup> quality of life (QOL),<sup>9,10</sup> and survival<sup>2,7,8</sup> are noted with continued smoking post diagnosis. Thus, it seems that smoking cessation at or after cancer diagnosis likely confers beneficial effects on some or all of these outcomes. Because most clinical trials fail to assess smoking status after registration, or fail to analyze these data even if they are collected, we are missing major opportunities to detect adverse effects of smoking and benefits of cessation during the course of treatment and across follow-up.<sup>11</sup> This may be of particular interest to study in patients treated with chemotherapy, given that smoking status is proving to affect differentially the response to some treatment agents via molecular alterations and effects on drug metabolism.<sup>12</sup>

The Michigan SPORE prospective cohort study provides the opportunity to analyze how changes in patient smoking behavior affected outcome variables and survival after pretreatment assessment. Duffy et al<sup>1</sup> report that participants were resurveyed every 3 months for 2 years and annually thereafter. Additional analysis of this data set will be of great interest. In the current article, survival curves on the basis of smoking status began to diverge sharply at the 1-year follow-up assessment. Never smokers had the best sustained survival through 5-year follow-up; current smokers fared the worst; and former smokers fell in between, but much closer to smokers. What would be interesting to learn from these data are the survival outcomes of those patients who quit smoking after diagnosis and remained abstinent, whom we predict would fare better. Also, what were the

survival outcomes among the former smokers (who were defined in this study as those abstinent for 1 month or longer), if relapse to smoking occurred? Finally, how did former smokers abstinent more than 1 year fare relative to recent quitters?

Unfortunately, clinical researchers have not used standard definitions of smoking status or smoking behavior, which complicates interpretation of data across trials. In particular, recent quitters (< 1 year) are often classified as current smokers,<sup>6,13</sup> in contrast to the Duffy et al report. Gritz et al<sup>11</sup> have proposed definitions and items on the basis of national surveys and further expand the discussion of standardization of terminology and analyses.

Cancer diagnosis and treatment present a teachable moment for health behavior change.<sup>14-16</sup> Smoking cessation is especially important, given the multiple benefits for cancer and other comorbidity and survival.<sup>12,15</sup> *Treating Tobacco Use and Dependence: 2008 Update—Clinical Practice Guideline* provides the standard of practice for smoking cessation treatment.<sup>17</sup> Tailoring to the special needs of cancer patients can be accomplished within the context of the guidelines relating to issues such as medication indications during cancer treatment and psychological issues related to patient and family distress.

At the M. D. Anderson Cancer Center, we have developed a comprehensive tobacco treatment program that offers state-of-the-art care for patients and their family members by providing cognitive-behavioral counseling, motivational interviewing, psychiatric consultation, nicotine replacement and tobacco-cessation prescription medications, and multisession follow-up at no cost.<sup>18</sup> The program is funded by the M. D. Anderson Cancer Center using tobacco settlement funds from the state of Texas. The program currently sees more than 700 patients per year, roughly 45% of whom present with comorbid alcohol use or mood disturbances. Although all physicians should be familiar with tobacco dependence and the basics of counseling,<sup>17,19</sup> this specialized clinical service assures the highest quality of treatment and sustained follow-up.

## ALCOHOL USE

In contrast to the extensive literature demonstrating numerous and significant adverse disease-related outcomes associated with continued tobacco use among head and neck cancer patients, much less is known about the effects of continued alcohol use after diagnosis and treatment. Although Stevens et al<sup>20</sup> and the Duffy study found no relationship between continued alcohol consumption and patient survival, other studies have found an increased risk of second primary tumors (SPTs) among continued drinkers with head and neck cancer.<sup>6,21</sup> For example, Do et al<sup>6</sup> described a dose-response relationship

between continued alcohol use and risk for SPTs, and reported a 50% increased risk of SPTs when alcohol consumption exceeded 14 drinks per week. The relationship between continued alcohol use and QOL after the diagnosis of head and neck cancer has not been fully characterized. Duffy et al<sup>22</sup> found no association between QOL and alcohol use among head and neck cancer patients. However, Allison<sup>23</sup> found alcohol use to be associated with improved health-related QOL: head and neck cancer patients consuming alcohol reported significantly better physical and role functioning, and less fatigue, pain, problems swallowing, dry mouth, and feelings of illness compared with patients who did not consume alcohol. At present, additional data are needed to describe the relationship between amount or frequency of alcohol intake and health outcomes in head and neck cancer survivors. Findings from SPORE may be able to shed additional light on the role of continued alcohol use in survival in functional and QOL outcomes for this population, as well as the degree to which effects are influenced by quantity and frequency of alcohol use. Notwithstanding such findings, Duffy et al discuss the need and appropriate timing of treatment for alcohol dependence relevant to smoking cessation.<sup>1</sup> In noncancer populations, evidence is mixed regarding the efficacy of simultaneous treatment.<sup>24,25</sup> In the only study to specifically target multiple risk behaviors in a head and neck cancer patient population, Duffy et al conducted a tailored smoking, alcohol, and depression intervention.<sup>26</sup> At 6-month follow-up, the smoking cessation quit rate was significantly higher in the intervention group compared with usual care. There were no significant differences in alcohol or depression outcomes between intervention and control groups. Clinical concerns have focused on adverse effects of concurrent treatment of smoking cessation on alcohol abstinence outcomes. Multiple risk-factor treatment warrants additional research on both behavioral and medical outcomes.

## DIET AND PHYSICAL ACTIVITY

Duffy et al also suggest that although premorbid diet and physical activity are associated with survival in univariate analyses, as with alcohol intake these factors fall out in multivariate models, and smoking remains the sole significant predictor.<sup>1</sup> Although such data are valuable, it remains unknown whether the practice of healthful diet or physical activity behaviors postdiagnosis are of benefit in reorienting survival trajectories. Given promising findings in other cancers, such as breast and colon cancer, such data would be of interest in patients with head and neck cancer.<sup>14,27</sup>

We therefore look forward to Duffy's future analysis of physical activity data collected throughout follow-up in relation to survival, but lament that follow-up data are not available for diet. Although overall survival alone is indeed a hard end point, it also is important to remember that significant associations have been reported between diet and exercise practices and other key outcomes such as comorbidity, functional status, and health-related QOL.<sup>14,27</sup>

The diet and exercise data of Duffy et al also lend additional support to the longstanding observation of behavioral clustering, which has been reported during the past several decades in healthy populations, as well as those diagnosed with cancer.<sup>27</sup> Data suggest that poor lifestyle practices do not occur independently or in isolation, but rather band together in a constellation. Thus, the study of Duffy et al is one of many showing that smokers not only have greater alcohol

use, but also have suboptimal diets and levels of physical activity. Their findings, however, are striking in that they show the magnitude of poor dietary intake and physical inactivity in this specific clinic population marked by mean intakes of fruits and vegetables that are at least one serving lower than the national average, and where the mean Physical Activity Scale for the Elderly index is roughly 30 points lower than the population norm of 144 for 55- to 64-year-old Americans.<sup>28,29</sup> Thus, head and neck cancer survivors who are current or former smokers represent a population in great need and, as Duffy et al point out, are not only in need for smoking cessation interventions, but for interventions that target multiple behaviors. To date, however, no trial has tested a multiple-component intervention that includes smoking cessation, diet, exercise, and possibly alcohol components among individuals diagnosed with cancer. Basic behavioral science research questions remain unanswered, such as the time during the course of survivorship when various interventions should be offered and the optimal sequence, the optimal channels, and the best setting for delivery, as well as the best person to deliver care. In the years ahead, the alliance between oncologists and behavioral scientists will be key in successfully developing, delivering, and assessing multiple interventions across the spectrum of cancer survivors.

## AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

## AUTHOR CONTRIBUTIONS

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