SMOKING CESSATION IN CANCER SURVIVORS: EXPLORING PSYCHOSOCIAL WELLBEING, BELIEFS ABOUT SMOKING, AND E-CIGARETTE USE

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ABSTRACT

Yael Rose Symes: Smoking cessation in cancer survivors: Exploring psychosocial wellbeing, beliefs about smoking, and e-cigarette use
(Under the direction of Shelley D. Golden)

Smoking after a cancer diagnosis is associated with various negative health outcomes and existing smoking cessation interventions for cancer survivors have not been effective in influencing cessation rates. The purpose of this dissertation is to better understand smoking-related factors uniquely influenced by receiving a cancer diagnosis that could be used to create more successful cessation interventions for cancer survivors.

Manuscript 1 used time-to-event analysis to assess whether psychosocial factors—distress, health-related quality of life (HRQOL), and perceived social support—at one year after diagnosis predicted whether survivors successfully quit smoking and the amount of time it took to quit in a longitudinal nationally representative sample of long-term cancer survivors from the American Cancer Society Study of Cancer Survivors (SCS-I; $n = 341$). Manuscript 2 assessed whether survivors of tobacco-related cancers reported higher perceived severity of health problems from smoking compared to survivors of non-tobacco-related cancers and explored whether this relationship was stronger for recently-diagnosed versus long-term survivors in a cross-sectional national sample from the Population Assessment of Tobacco Health—PATH—study ($n = 433$). Manuscript 3 identified e-cigarette use prevalence and reasons for use among

cancer survivors who smoke (n = 433) and compared to smokers without a prior cancer diagnosis (n = 10,872) in the PATH study.

In Manuscript 1, survivors with low physical HRQOL were significantly less likely to quit smoking and took several more years to quit than survivors with high physical HRQOL. In Manuscript 2, survivors of tobacco-related cancer reported higher perceived severity of smoking than survivors of non-tobacco-related cancer and this relationship was the same for recently-diagnosed and for long-term survivors. In Manuscript 3, nearly 6 in 10 cancer survivors who smoke had used e-cigarettes, and nearly one quarter of survivors were currently doing so; rates were similar in those never diagnosed. The majority of both groups (>71%) reported using e-cigarettes for perceived health-related reasons—including smoking reduction.

Clinicians may want to assess physical HRQOL, perceived severity of smoking, and discuss the research on the efficacy of e-cigarettes as a quitting strategy with their patients who smoke to identify patients at particularly high risk of continued smoking and potential means for interventions.

To Jeff and Evelyn

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CHAPTER 1: OVERVIEW AND SIGNIFICANCE

1.1 Purpose of Dissertation

Cancer survivors—particularly survivors of tobacco-related cancers (e.g., lung and head and neck)—smoke at higher rates than the general population.[1] Smoking after a cancer diagnosis is associated with lower rates of survival, higher rates of recurrent disease and secondary tumors, and decreased efficacy of treatment.[2-6] The purpose of this dissertation is to better understand smoking-related factors uniquely influenced by receiving a cancer diagnosis that could be targeted in smoking cessation interventions to improve quit rates and ultimately reduce morbidity and mortality outcomes in this population. This dissertation examines psychosocial predictors of both quitting smoking and the length of time it takes to quit, diagnosis of a tobacco-related cancer as a correlate of beliefs about the harms of smoking, and the use of a perceived harm reduction strategy—e-cigarettes—in cancer survivors who smoke. Manuscript 1 uses time-to-event analysis to assess whether psychosocial factors (e.g., psychological distress, health-related quality of life, perceived social support) at one year after diagnosis predict whether survivors successfully quit smoking and the amount of time it takes a survivor to quit in a longitudinal nationally representative sample of long-term cancer survivors diagnosed within 10 years. Manuscript 2 assesses whether survivors of tobacco-related cancers report higher perceived severity of health problems from smoking compared to survivors of non-tobacco-related cancers in a cross-sectional national sample of survivors. This paper further explores whether the observed relationship between diagnosis of tobacco-related cancer and perceived severity of

smoking varies by time since diagnosis (i.e., if the relationship is stronger for recently-diagnosed versus long-term survivors). Last, Manuscript 3 documents e-cigarette use and reasons for e-cigarette use among cancer survivors who are also smokers of combustible cigarettes, and compares the prevalence and reasons for use to those for smokers never diagnosed with cancer.

The knowledge gained from this dissertation will provide guidance for interventions that could be designed specifically for cancer survivors. For example, if psychosocial factors such as health-related quality of life (HRQOL) strongly predict if and when survivors quit after diagnosis, then smoking cessation interventions could target survivors with poor HRQOL with more intensive long-term support. Additionally, if survivors of tobacco-related cancers perceive higher severity of health problems from smoking than survivors of non-tobacco-related cancers, this suggests that interventions need to especially target the beliefs of survivors of non-tobacco-related cancers. Finally, it would be useful for clinicians to know if cancer survivors who smoke are using e-cigarettes as a possible smoking cessation tool, so that misconceptions about the cessation efficacy and harms of e-cigarettes can be addressed in clinical encounters. In sum, the knowledge from this dissertation will inform which modifiable outcomes and subpopulations to target in smoking cessation interventions to better meet the needs of cancer survivors.

1.2 The Problem of Smoking After Cancer Diagnosis

The smoking prevalence of cancer survivors after diagnosis ranges widely from 7-51%[1,7-10] because the prevalence differs by type of cancer.[10] Survivors of tobacco-related cancers (e.g., cervical,[1,11-13] bladder,[13] and lung cancer[13]) report the highest rates of smoking, in part because they were more likely to smoke before diagnosis.[13] Cervical cancer survivors smoke at the highest rates of any cancer site—with rates ranging from 33-51%.[1,11,13] One large national study in the United States that included cancer survivors with a wide range of years since diagnosis

found that 27% of bladder cancer survivors smoke after diagnosis compared to 23.5% of lung cancer survivors.[13] Smoking rates are lowest in prostate, breast, colon, and melanoma cancer survivors, who smoke at rates ranging from 7-12%.[1,11,12] Depending on cancer site, the smoking rate in cancer survivors as a group is as high or higher than the smoking rate of the general United States population,[10] which the Centers for Disease Control and Prevention (CDC) estimate to be 15%.[14]

Smoking after a cancer diagnosis is associated with various negative health outcomes. A recent review of the negative consequences of smoking after cancer diagnosis reported that current smoking is associated with lower survival in lung, head and neck, breast, prostate, esophageal, cervical, endometrial, bladder, ovarian, leukemia, and lymphoma cancer patients.[15] Additionally, smoking after cancer is related to higher rates of recurrent disease[5,16,17] and more primary tumors.[16-23] Continued smoking after cancer diagnosis is also associated with decreased efficacy of cancer treatment,[3,17] increased treatment-related complications and symptom burden (e.g., more sleep problems, higher pain severity, more fatigue),[6,15,17,24-27] and lower HRQOL.[15,27-30] Those who smoke after a cancer diagnosis also have an increased risk for comorbid conditions such as myocardial infarction, congestive heart failure, and diabetes.[15,18,31] Thus, the morbidity and mortality associated with smoking after a cancer diagnosis constitutes a significant public health problem.

1.3 Smoking Cessation

There are multiple health benefits of quitting smoking, and the percentage of cancer survivors who smoke and who want to quit ranges from 49-69%.[11,12,32,33] Tobacco dependence is a chronic disease that often requires multiple quit attempts and repeated intervention to alter.[34] The majority of tobacco users will experience multiple periods of *relapse* (i.e., a return to regular

smoking)—up to 80% of smokers relapse.[35] There is a distinction between "relapse" and a "lapse" or "slip": the latter refers to a brief return to smoking that does not turn into regular smoking.[34] Smoking cessation is commonly measured as *continuous abstinence*, which refers to when participants in a study do not smoke from their quit date to a designated outcome point (e.g., 6 months after the quit date).[34] Smoking cessation is also commonly measured as a *point prevalence*—i.e., tobacco use occurrence within a set period (usually 7 days).[34] Smoking cessation in this dissertation refers to whether someone who had been a regular smoker reported that they had completely quit smoking.

1.4 Significance of the Research

There is a paucity of smoking cessation treatment programs in oncology settings.[15,36] A recent meta-analysis of 10 randomized-controlled trials found that the few smoking cessation interventions for cancer survivors that have been implemented did not significantly influence smoking cessation rates in both the short and long term.[37] A meta-analysis of randomized-controlled trials found that cessation intervention strategies that were effective in the general population were not effective in cancer survivors (Sheeran et al., under review). The authors of three systematic reviews of smoking cessation interventions for cancer survivors recommend that cancer survivors receive the gold standard for smoking cessation treatment in the general population: a combination of medication—mainly nicotine replacement therapy (NRT) and varenicline— and behavioral therapies such as counseling and reading materials.[37-39] Yet cancer survivors might have unique needs, motivations, and beliefs about smoking that could influence quitting outcomes, and should therefore be incorporated into quitting interventions designed for them. This dissertation identifies factors that might be important to target in smoking cessation interventions designed specifically for cancer survivors. For instance, understanding factors

particularly relevant to cancer survivors (e.g., poor psychosocial wellbeing or specific cancer types) could help public health professionals identify the survivors most in need of intensive cessation interventions. Additionally, knowing if cancer survivors are more prone to trying e-cigarettes as a cessation aid can prompt patient-provider discussions about the evidence of the efficacy and harms of e-cigarettes. This knowledge could better equip healthcare clinicians in their recommendations for smoking cessation strategies for their patients. This dissertation investigates several risk factors and cessation strategies among cancer survivors who smoke that could illuminate ways to create more effective smoking cessation interventions: psychosocial factors including distress, perceived social support, HRQOL; cancer type (tobacco-related or non-tobacco-related) and perceived severity of harms from smoking; and e-cigarette use and reasons for use.

Manuscript 1: Psychosocial Factors and Smoking Cessation in Long Term Survivors.

Karam-Hage and colleagues argue for the need for smoking cessation interventions to be tailored to the specific needs of cancer survivors, paying special attention to psychosocial factors that can interfere with tobacco cessation treatments as well as treatments for cancer.[39] There are several potential psychosocial predictors of smoking outcomes in the general population—including psychological distress, HRQOL, and perceived social support[40-42]—that are likely directly affected by receiving a cancer diagnosis.[43-45] Understanding who is most at risk for continuing to smoke after a cancer diagnosis based on measures of psychosocial wellbeing will allow public health professionals to know whom to deliver more intensive cessation interventions. Also, knowing if these psychosocial factors predict how long it takes survivors to quit could help clinicians identify ideal times for cessation support in the years following after diagnosis. Japuntich et al. stress the need for studies to evaluate the relationship between

psychosocial functioning and smoking cessation outcomes in longer-term survivors, because of the high rate of smoking relapse in this group.[46] It takes survivors on average 8.8 years to successfully quit after diagnosis[47] and many survivors make multiple quit attempts.[34,46,48] Understanding the trajectory of cessation among those survivors who do not quit smoking immediately after diagnosis, and whether psychosocial factors that can be assessed as part of routine healthcare screening predict that trajectory, can guide the type and timing of clinician cessation support. Manuscript One of this dissertation uses time-to-event analysis in a longitudinal national dataset to investigate the following research question:

> **Research Question 1.1:** Do psychosocial factors at one year after diagnosis predict whether survivors quit and the length of time it took to quit smoking within 10 years from diagnosis?

Manuscript 2: Diagnosis of Tobacco-Related Cancer and Perceived Severity of Health Problems from Smoking.

Although initial smoking rates are higher among those diagnosed with a tobacco-related cancer, several studies have found that smokers who are diagnosed with tobacco-related cancers quit smoking at higher rates than smokers diagnosed with other cancer types.[47,49,50] There is little investigation of mechanisms that might explain the difference in quit rates between survivors of tobacco-related and non-tobacco-related cancers. Higher perceived severity of health problems from smoking (e.g., believing that smoking is harmful to health) is associated with smoking cessation in cancer survivors[49,51] and might help explain the relationship between cancer type and smoking cessation. Survivors of tobacco-related cancers might have higher perceived severity of health problems from smoking than survivors of non-tobacco-related cancers if they are more likely to attribute their cancer to their tobacco use and if they are more likely to be advised by their loved ones and clinicians to quit. If survivors of non-tobacco-related cancers

have lower perceived severity of the harms of continued smoking, then cessation efforts could focus on changing the smoking beliefs of this group. Further, it is possible that this difference in perceived severity between the two groups is particularly pronounced immediately following diagnosis when health and mortality are most salient. This knowledge could further inform how to help cancer survivors quit smoking years after they are diagnosed, for example, by focusing intervention efforts to increase perceived severity of health problems from smoking in survivors of non-tobacco-related cancers soon after diagnosis when their perceived severity is significantly lower than that of survivors of tobacco-related cancers. Manuscript Two investigates the following research question:

> **Research Question 2.1:** Among current smokers, do survivors of tobacco-related cancers report higher perceived severity of health problems from smoking than survivors of non-tobacco-related cancers and does the relationship between diagnosis of tobacco-related cancer and perceived severity from smoking vary by time since diagnosis?

Manuscript 3: Dual cigarette and e-cigarette use in cancer survivors

Cancer survivors who smoke, as compared to smokers without cancer, are particularly motivated to quit smoking.[39] Smokers in the general population often perceive and use e-cigarettes (also known as electronic cigarettes, electronic nicotine delivery systems—ENDS, and vapor pens) as a strategy to reduce or eliminate combustible cigarette use,[52-54] but research on whether cancer survivors do the same is limited. The evidence of e-cigarettes as a successful quit strategy is modest and controversial. Meta-analyses that have included the results of observational and randomized control trials found that e-cigarette use was associated with significantly *lower* odds of quitting smoking combustible cigarettes,[55,56] yet other meta-analyses which included only randomized control studies found that e-cigarette users were *more* likely to

quit if their e-cigarettes contained nicotine versus if they did not contain nicotine.[57,58] There is one published randomized control trial that compared e-cigarettes to another smoking cessation method—nicotine replacement therapy (NRT), but this trial did not find significant differences between the two intervention arms and[59] and had significant methodological limitations.[56] Thus, as the literature stands, there is inconclusive evidence that e-cigarettes help smokers—including both cancer survivors and those never diagnosed—quit combustible cigarettes. In addition to the limited efficacy of e-cigarettes as a smoking cessation tool, there are known short-term harms of e-cigarette use (e.g., burns and other injuries),[60] although more research is needed to document long-term health consequences of using e-cigarettes specifically in cancer survivors, including the potential adverse interactions of e-cigarettes and cancer therapies.[61] The authors of three systematic reviews of smoking cessation interventions for cancer survivors recommend that cancer survivors receive evidence-based cessation support including a combination of FDA-approved medication—mainly nicotine replacement therapy and varenicline— and behavioral therapies such as counseling and reading materials.[37-39]

Little is known about e-cigarette use and reasons for use among cancer survivors who want to quit smoking conventional cigarettes and who might be more motivated to use e-cigarettes as a smoking cessation or reduction tool than those without a history of cancer. There is only one published study (by Kruse et al.) to my knowledge that statistically compared differences in ever and current e-cigarette use between currently smoking cancer survivors and a population never diagnosed with cancer.[62] Kruse and colleagues found that among current smokers, ever and current e-cigarette use were not different between cancer survivors and the population without a medical comorbidity.[62] This study, however, did not consider demographic differences between the two groups. The majority (87%) of cancer survivors in the U.S. are

diagnosed at or over age 50,[63] whereas younger age is associated with higher e-cigarette ever use.[64,65] It might be important to account for differences in age to determine whether survivors are using e-cigarettes at rates beyond what we would expect for their age group. There is also no research on differences in e-cigarette use by cancer type. Survivors of tobacco-related cancers might be differentially motivated to quit smoking combustible cigarettes because of the well-known association between smoking and tobacco-related cancers (e.g., lung cancer). Last, there are no studies to our knowledge that detail the various reasons that cancer survivors report using e-cigarettes and how these reasons compare to those of a general population of smokers. If e-cigarette use rates are relatively high for cancer survivors, and particularly for survivors of specific tobacco-related cancers, then clinicians who treat cancer survivors may need to discuss the current evidence about the cessation efficacy and harms of e-cigarettes with their patients who are trying to quit or reduce smoking. Manuscript Three of this dissertation explores the following research questions:

> **Research Question 3.1:** Does the prevalence of e-cigarette use among current combustible cigarette smokers vary by cancer survivorship status and cancer type?
>
> **Research Question 3.2:** Do reasons for e-cigarette use among current combustible cigarette smokers vary by cancer survivorship status?

CHAPTER 2: THEORETICAL FRAMEWORK

2.1 Constructs from Three Health Behavior Theories

The theoretical model of the first manuscript in this dissertation outlines mechanisms that might explain how psychosocial factors are related to both receiving a cancer diagnosis and to smoking cessation outcomes, including quitting and the length of time it takes to quit. The model is informed by the Health Belief Model (HBM),[66] the Theory of Planned Behavior (TPB),[67] and the Cognitive-Social Health Information Processing model (C-SHIP).[68,69] The theoretical model of the second manuscript in this dissertation illustrates how the perceived severity of health problems from smoking could explain the relationship between a diagnosis of tobacco-related cancer and smoking cessation, and is informed by the HBM and the C-SHIP model. The research questions of manuscript three of this dissertation are exploratory, and thus do not have a theoretical underpinning.

The HBM is a value expectancy theory that assumes individuals are rationally motivated to perform a health behavior to avoid negative health outcomes.[66] The central premise of the HBM is that individuals' beliefs about costs and benefits of a health behavior combined with their perceived threat of inaction (i.e., perceived severity and susceptibility) and their self-efficacy for the specific behavior, predicts whether or not that person will perform the behavior. The TPB assumes that the best predictor of a health behavior is the intention to perform that behavior, which is determined by the attitude toward the behavior (i.e., benefits and barriers), the perception of social norms regarding the behavior, and perceived control over the performance of

the behavior.[67] The C-SHIP model is an overarching theoretical framework specific to cancer prevention and control that describes how individuals cognitively and affectively process health information and how this information translates into health behaviors.[68,69] Before a cancer survivor engages in efforts to quit smoking, according to C-SHIP, the survivor evaluates their health beliefs, expectancies, values, goals, and affective response. For example, a survivor might quit smoking only if they perceive that their health will be at risk if they continue to smoke and that they will improve their health if they quit smoking.

The combination of constructs from the HBM, the TPB, and the C-SHIP model provides an overall framework that recognizes the importance of attitudinal beliefs (i.e., perceived benefits and barriers of quitting), the perceived severity of health problems from smoking, and the intention to quit smoking in smoking cessation. Several constructs from each of these theories overlap, but they all stress the importance of beliefs about engaging in the behavior (e.g., quitting smoking) and the outcomes of the behavior. All of constructs from each of the three theories and their potential relevance to smoking cessation in cancer survivors are summarized in Table 2.1. My goal was to develop conceptual models that illustrated potential links between psychosocial variables (Manuscript 1) and cancer type (Manuscript 2) and cessation behaviors in cancer survivors, rather than to test all potential predictors of cessation. I therefore identified constructs from Table 2.1 that were the most plausible links between the ideas I explored in each manuscript. As a result, I did not employ all constructs for any one theory, and several key components of some theories (e.g., self efficacy, perceived behavioral control, subjective norms) were not part of my conceptual models.

Additionally, several researchers have argued that the constructs I chose to include in the theoretical models for Manuscripts 1-2 are critical constructs related to smoking cessation

outcomes in cancer survivors. In one study, Westmaas and colleagues found that the odds of quitting smoking in survivors were higher for those with higher perceived severity of smoking-related health problems and those who perceived more benefits of quitting. In that study, the odds of quitting smoking were lower for survivors who perceived more barriers to quitting.[70] Another study that identified correlates of continued smoking after diagnosis in head, neck, and lung cancer patients found that smokers, compared to those who quit, reported lower risk perceptions (i.e., lower awareness of the adverse health effects associated with continued smoking), lower benefits of quitting, and higher barriers to quitting.[51] In a study of patients of mixed cancer types, current smokers with intentions to quit had higher perceived health risks of smoking than current smokers with no intention to quit smoking.[71] A qualitative study of lung, liver, stomach, nasopharynx, or colorectal cancer survivors found that an important barrier to quitting smoking in current smokers was limited perceived benefits to quitting and the perception that the barriers to quitting outweighed the benefits.[72] Berg and colleagues explained that smoking behavior in cancer survivors results from the intention to smoke, which is a function of attitudes toward smoking.[8] In sum, attitudes about quitting, perceived severity of health problems from smoking, and the intention to quit smoking are all important constructs that could influence smoking cessation outcomes in cancer survivors.

Table 2.1: Theoretical Constructs

Theory	Construct	Definition	Relevance
HBM	Perceived susceptibility	Belief about the risk of getting a disease (part of perceived threat)	Cancer survivors with high social support might be more likely to perceive they are susceptible to health harms if they continue smoking if their social network advises them to quit.
	Perceived severity	Belief about the health consequences of the behavior/disease (part of perceived threat)	A cancer survivor's social network can provide health information about the health risks of continued smoking after diagnosis (e.g., death), which in turn could increase a survivor's perceived severity of health problems from smoking. Survivors of tobacco-related cancer might report higher perceived severity of smoking than survivors of non-tobacco-related cancer.
	Perceived benefits	Belief in the efficacy of the behavior to reduce harm	Survivors with high distress and low HRQOL might perceive the benefits of quitting to be low if they use smoking as a way to cope. Those with high social support might learn about the pros of quitting (e.g., to improve health and prevent disease) from their social network.
	Perceived barriers	Belief about costs (tangible and psychological) of the behavior	Survivors with high distress and low HRQOL may not feel that they are able to quit smoking because they do not have other resources to cope. The barriers of quitting might also outweigh the benefits for those who are trying to quit but who have consistently relapsed, because relapsing may add to distress. Low social support could be a barrier to quitting if survivors perceive they have no one to help them quit.
	Cues to action	Strategies to instigate action	Survivors with high social support might receive reminders to quit from their social network.

Theory	Construct	Definition	Relevance
	Self-efficacy	Confidence in one's ability to take action	Survivors with high social support might have higher self-efficacy to quit smoking if they know they have people they can rely on to help them quit.
TPB	Attitude	Beliefs about performing the behavior (evaluation of behavioral outcomes)	Survivors with high distress and low HRQOL might have more negative beliefs about quitting if they use smoking as a way to cope. Those with high social support might have more positive attitudes about quitting if their social network encourages them to quit.
	Subjective norm	Includes normative beliefs (how important individuals in social network feel about the behavior) and motivation to comply to norms	Survivors with high social support might be exposed to more normative beliefs about quitting if their loved ones advise them to quit. Survivors with high social support might also be motivated to comply to norms if they do not want to let their loved ones down. Survivors of tobacco-related cancer might also feel more normative pressure to quit from their loved ones.
	Perceived behavioral control	Factors outside individual control that may affect intentions and behaviors (barriers and extent barriers will make it difficult to perform the behavior) and agency to perform the behavior.	Survivors with high distress and low HRQOL may not have other coping resources to help them quit. The barriers of quitting might also outweigh the benefits for those who are trying to quit but who have consistently relapsed, because relapsing may be add to distress. Low social support could be a barrier to quitting.

Theory	Construct	Definition	Relevance
	Intention to perform behavior	Deciding to perform behavior; the most important determinant of the behavior	It is possible that survivors with poor psychosocial functioning take longer to quit because it might take them longer to decide to make a serious quit attempt (because of different attitudes about quitting and perceived severity) than survivors with better psychosocial functioning. Survivors of tobacco-related cancer might be more likely to intend to quit than survivors of non-tobacco-related cancer.
CSHIP	Health-relevant encodings and construals	Strategies and constructs for encoding health risks (perceived vulnerability)	Cancer survivors with high social support might be more likely to perceive threats to continued smoking if their social network advises them to quit.
	Health beliefs and expectancies	Specific beliefs and expectations activated in health information processing. Includes expectancies about outcomes and self-efficacy expectancies	Survivors with better psychosocial functioning might be more likely to believe they will improve their health if they quit. Survivors with high social support might have higher self-efficacy to quit smoking if they know they have people they can rely on to help them quit.
	Affects	Emotions	Survivors with poor HRQOL and high distress may feel anxious, ashamed, hopeless, and fatalistic about quitting.
	Health goals and values	Desired health outcomes and their importance and goals for achieving these outcomes	Survivors with better psychosocial functioning may feel it is important to live a good quality of life, and decide to quit smoking to achieve optimal health, whereas survivors with worse psychosocial functioning may feel it not worthwhile to take steps to prolong their lives.

2.2 Theoretical Application In Manuscripts 1 and 2

Manuscript 1: Psychosocial Factors and Quitting Smoking in Long-Term Cancer Survivors.

Psychosocial factors—specifically a survivor's level of psychological distress, HRQOL, and perceived social support—might be particularly important in shaping smoking-related beliefs in cancer survivors because many survivors face unique issues precipitated by their cancer diagnosis and treatment that might impact psychosocial wellbeing (e.g., feelings of guilt, shame, fear of recurrence, reduced HRQOL, and social isolation). These psychosocial factors also likely influence attitudes (benefits and barriers to quitting smoking) and the perceived severity of health problems from smoking and in turn, intentions to quit smoking, which influence quitting outcomes.

A cancer diagnosis can cause distress in the form of anxiety, fear of recurrence, and feelings of guilt, stigma or shame—which can last for years after diagnosis.[43,73,74] Distress might influence a person's attitudes (i.e., benefits and barriers) of smoking cessation. Those who are distressed may not feel that they are able to quit smoking because they do not have other resources to cope with their cancer-related stress; thus the lack of coping resources acts as a major barrier to quitting. Cancer survivors might use smoking as a way to cope with cancer-related stress. Those who self-medicate their distress with smoking might perceive the benefits of quitting to be low if they use smoking as a way to cope. The barriers of quitting might also outweigh the benefits for those who are trying to quit but who have consistently relapsed, because relapsing may be add to distress. Indeed, in a healthy population, current smokers who made an unsuccessful quit attempt in the past year reported higher levels of psychological distress than those who did not report making an unsuccessful quit attempt.[75] The negative feelings from an anticipated possible relapse might also be a strong barrier to quitting.

Many cancer survivors will experience reductions in HRQOL, which can include pain, fatigue, respiratory problems, changes in body image, problems in sexual functioning at some point after diagnosis that can persist for years after they are diagnosed.[44,76] A cancer survivor's HRQOL might influence their attitudes toward smoking cessation. For example, the benefits of quitting might be to low and the barriers of quitting might be high if survivors with poor HRQOL use smoking as a way to cope with their physical limitations.

Individuals diagnosed with cancer often receive an initially high level of social support at the time of diagnosis, but over time this support often diminishes and some cancer patients become socially isolated after treatment ends,[77] which can make it more difficult for them to get the support they need to help them quit smoking. Social support can directly and indirectly influence smoking cessation. In the direct link, social resources can be a source of motivation and reinforcement to quit.[78] Westmaas and colleagues argue that the functions of social support can be specific to smoking abstinence.[79] For instance, informational support can include advice about how to cope with withdrawal or general advice on how to cope with stress; emotional support can include listening to the venting of emotions about the difficulty of quitting or about stressful emotions in general; and instrumental support can consist of providing nicotine replacement therapy or helping the person with chores that might reduce their overall stress and distract them from smoking.[79] These functions of social support could also influence smoking cessation indirectly by shaping a cancer survivor's perceived severity of smoking and attitudes (i.e., perceived benefits and barriers to quitting). A cancer survivor's social network can provide health information about the health risks of continued smoking after diagnosis, which in turn could increase a survivor's perceived severity of health problems from smoking. Cancer survivors' attitudes about smoking could also be influenced by social support. A study of 290

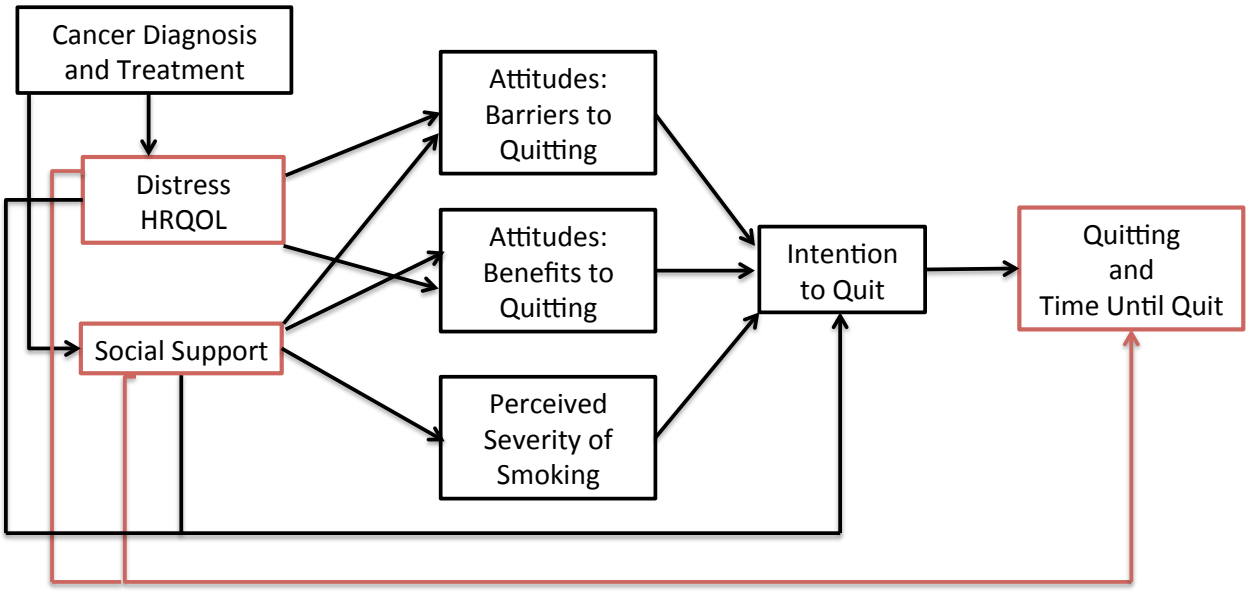
adults found that emotional and instrumental support provided by a close family member or friend was significantly associated with behavioral intention to perform goal behaviors specific to each participant and attaining the goal behavior.[80] The authors of that study argue that aspects of social support are likely associated with the precursors to behavioral intention (e.g., attitude about the behavior). There are no studies to my knowledge that specifically tested if perceived social support is associated with attitudes and perceived severity of health problems from smoking in the general population or in cancer survivors. However, Zhang and colleagues found that the effects of received social support for leisure time physical activity on intention to perform physical activity were mediated by attitudes on physical activity.[81] Thus, perceived social support likely directly and indirectly influences behaviors such as smoking cessation by shaping perceived severity of health problems from smoking and attitudes toward smoking.

In sum, many cancer survivors experience issues related to their diagnosis and treatment (e.g., guilt and shame related to their diagnosis, fear of disease recurrence, physical limitations, and social isolation), which can reduce their psychosocial health (i.e., increase distress, reduce HRQOL and perceived social support). Poor psychosocial functioning in turn could reduce negative attitudes about quitting and perceived severity of health problems from smoking, which could reduce their intention to quit smoking and likelihood of successfully quitting.

Although less research examines the length of time it takes to quit smoking, this outcome may also be associated with quit intentions. It is possible that cancer survivors with worse psychosocial functioning, who perhaps have more negative attitudes about quitting, more positive attitudes about smoking, and lower perceived severity of harms from smoking, might experience more periods of relapse and thus take longer to quit smoking than survivors with better psychosocial functioning. It is also possible that survivors with poor psychosocial

functioning take longer to quit because it might take them longer to decide to make a serious quit attempt than survivors with better psychosocial functioning.

Theoretical Conceptual Model for Manuscript 1

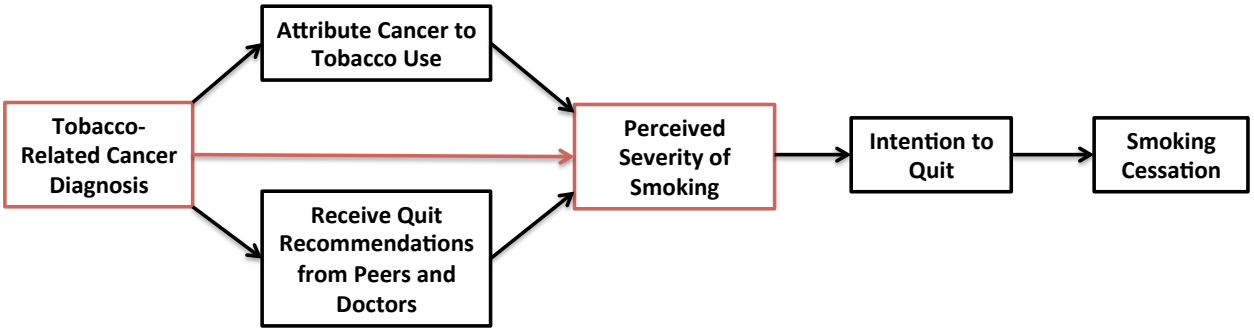


Manuscript 2: Diagnosis of Tobacco-Related Cancer and Perceived Severity of Health Problems from Smoking.

The perceived severity of health problems from smoking is an important precursor to quitting smoking. Perceived severity of health problems from smoking might help explain the relationship between diagnosis of tobacco-related cancer and smoking cessation. If survivors of tobacco-related cancers have higher perceived severity of health problems from smoking compared to survivors of non-tobacco-related cancers, they might be more likely to have an intention to quit and thus quit at higher rates. The health risks of smoking after diagnosis might be especially salient to survivors of tobacco-related cancers because of the well-known link between tobacco use and lung and head and neck cancer. Survivors of tobacco-related cancer who attribute their cancer diagnosis to their own tobacco use might perceive higher severity of health problems from smoking than survivors of non-tobacco-related cancers who might not

attribute their cancer to tobacco use. In addition, many survivors of tobacco-related cancer might be advised by their loved ones and healthcare clinicians to quit, which in turn might promote higher perceived severity of smoking than survivors of non-tobacco related cancers who are perhaps not as frequently advised by their healthcare clinicians to quit. A clinician's advice to quit is as an important motivator for quit attempts in the general population of smokers.[34,82,83]

Theoretical Conceptual Model for Manuscript 2



CHAPTER 3: MANUSCRIPT 1-
THE IMPACT OF PSYCHOSOCIAL FACTORS IN PREDICTING SMOKING CESSATION IN LONG-TERM CANCER SURVIVORS: A TIME-TO-EVENT ANALYSIS

Objective. Smoking poses significant health risks to cancer survivors. Receiving a cancer diagnosis may heighten distress, and reduce social support and health-related quality of life (HRQOL), each of which could inhibit successful smoking cessation. Understanding longitudinal associations between these psychosocial factors and successful cessation could help clinicians better tailor cessation interventions for their patients. **Methods**. We conducted time-to-event analyses using data from the American Cancer Society Study of Cancer Survivors-I (SCS-I)—a longitudinal nationwide study—to examine the relationship between psychosocial factors and cessation likelihood in cancer survivors diagnosed 7-10 years prior. We also assessed whether psychosocial factors were associated with the amount of time it took survivors to quit following diagnosis. **Results**. Cancer survivors with high physical HRQOL were more likely to quit smoking within 10 years of their cancer diagnosis than survivors with low physical HRQOL, controlling for cancer type and number of comorbid conditions at baseline (HR = 1.96; 95% CI: 1.10-2.70; p=.02). Survivors with high physical HRQOL also took less time to quit than survivors with low physical HRQOL. Survivors of tobacco-related cancers with low physical HRQOL were the least likely group to quit. No significant relationships between the other psychosocial predictors and cessation outcomes were observed. **Conclusions**. Smoking cessation programs are needed for all cancer survivors who smoke, but survivors with low physical HRQOL may need even more intensive long-term smoking cessation interventions with multiple

check-in points after smoking relapses. Cessation interventions that include strategies to mitigate physical symptoms in those with poor physical HRQOL deserve consideration in research and practice.

Introduction

The prevalence of smoking among cancer survivors ranges widely, from 7% to 51%, depending on the type of cancer.[1,8] Researchers estimate that between 14% to 64% of cancer survivors who smoked prior to their cancer diagnosis continue to smoke after their diagnosis.[7,10,47,84] Smoking after a cancer diagnosis is associated with various adverse health outcomes including lower survival,[2,4] higher rates of recurrent disease,[5] more new primary cancers,[21] decreased efficacy of cancer treatment,[3] increased treatment-related complications and symptom burden,[6] and lower health-related quality of life (HRQOL).[27,29] There is a paucity of smoking cessation treatment programs in oncology settings[15,36] and a meta-analysis of randomized-controlled trials found that current smoking interventions for cancer survivors were ineffective, despite that fact that cessation interventions do work for the general population (Sheeran et al., under review). Thus, cancer survivors might have unique needs that could influence quitting outcomes, and understanding factors distinctly influenced by receiving a cancer diagnosis could help create more successful smoking cessation interventions for cancer survivors.

There are several psychosocial factors that are related to smoking status in the general population of smokers—including psychological distress, health-related quality of life (HRQOL), and perceived social support.[40-42] These psychosocial factors are also directly affected by receiving a cancer diagnosis.[43-45]

Psychological Distress

The diagnosis of cancer and the threat to life associated with it can be anxiety-provoking to many patients,[73] possibly making more difficult for those who smoke to quit. Many survivors of various cancers experience a fear of disease recurrence, which can be lasting and psychologically distressing.[43] Some cancer patients might feel stigma, guilt, or shame because of their diagnosis—especially if they feel they have caused their cancer by smoking.[74] Many people use tobacco as a way to cope with distress and regulate mood[85] and cancer survivors with high distress may feel that they do not have sufficient resources to cope with their cancer-related distress. One study with head and neck cancer patients found that continuing to smoke after diagnosis was associated with higher distress one year later, although no work has investigated distress as a predictor of cessation over long periods of time in cancer surivors.[86]

Health-Related Quality of Life (HRQOL)

Many cancer survivors experience reductions in HRQOL (i.e., a person's self-rated perception of health, which can include pain, fatigue, respiratory problems, changes in body image, problems in sexual functioning),[87,88] at some point after they are diagnosed, which can persist for years.[44,76] A systematic review of cross-sectional studies of lung cancer survivors found that continued smoking was associated with lower physical and mental HRQOL.[76] In a national survey, Blanchard et al. found that breast, prostate, and colorectal survivors diagnosed within 10 years who did not smoke had significantly higher HRQOL than those who did.[89] There have been no studies to our knowledge that have prospectively tested whether HRQOL predicts smoking cessation after cancer diagnosis.

Perceived Social Support

Individuals diagnosed with cancer often receive an initially high level of social support at the time of diagnosis, but over time this support often diminishes and some cancer patients become socially isolated after treatment ends,[77] which can make it more difficult for them to get the support they need to help them quit smoking. A longitudinal study found that breast cancer patients reported larger decreases in perceived social support (i.e., a person's perception of the resources available to them from their social interactions)[45] after two years from diagnosis compared to age-matched controls who reported more stable social support during that time.[90] Another longitudinal study that followed newly diagnosed survivors found that perceived emotional support decreased during the year after diagnosis.[91] Perceived social support can be a source of motivation and reinforcement to quit smoking.[78] In a cross-sectional analysis, lower levels of perceived emotional social support were associated with smoking after diagnosis in a sample of lung cancer patients.[92] A cross-sectional study of short and long-term survivors of various cancer types found that higher perceived social support was associated with higher odds of quitting smoking after diagnosis.[50] Longitudinal research is needed to assess the relationship between perceived social support and smoking cessation after diagnosis in long-term cancer survivors.

Overview of Current Study

Most investigations on psychosocial factors and smoking cessation in cancer survivors have been cross-sectional and focused on recently treated survivors of specific cancers.[93] Not much is known about whether psychosocial factors such as distress, HRQOL or perceived social support predict smoking cessation in long-term survivors of various cancer types. Survivors on average take 8.8 years to successfully quit after diagnosis among those who have quit[47] and

many make multiple quit attempts.[46] It is common for survivors who quit smoking immediately after diagnosis to later experience a smoking relapse after they complete their cancer treatment.[94] Identifying psychosocial risk factors associated with continued smoking after a cancer diagnosis, which could be easily assessed as part of routine clinical care, could help public health professionals identify the survivors most in need of intensive cessation interventions. Additionally, knowing if these psychosocial factors predict how long it takes survivors to quit could help clinicians identify ideal times for cessation support in the years following after diagnosis. For example, smoking intervention efforts delivered immediately post diagnosis may need to be extended, especially among those with poor psychosocial functioning.

The present study uses time-to-event analyses in a longitudinal dataset of cancer survivors to examine if psychosocial factors assessed one year after diagnosis predict: 1) whether cancer survivors quit smoking after diagnosis and 2) how the probability of quitting changes over time. We adjust for the type of cancer diagnosis—whether a cancer is tobacco-related or not—and number of comorbidities (e.g., heart disease, diabetes, breathing problems) because these are medical factors uniquely related to smoking cessation in cancer survivors.[47,49] We hypothesize that survivors with higher psychological distress, lower HRQOL, and lower perceived social support at one year after diagnosis will be less likely to quit smoking and will take longer to quit compared to those with lower psychological distress, higher HRQOL, and higher perceived social support.

Methods

Data Source and Sample

We tested our hypotheses using data from participants represented in both Wave 1 and 3 of the American Cancer Society Study of Cancer Survivors-I (SCS-I). This longitudinal

nationwide study surveyed cancer survivors by mail or telephone roughly 1, 2, and 9 years after diagnosis. Wave 1 data were collected between 2000 and 2003, and Wave 3 data were collected between 2010 and 2011. Cancer survivors were selected through stratified random sampling of 11 state cancer registries. To be eligible for this study, survivors had to be at least 18 years old at diagnosis; diagnosed with one of the 10 most highly incident cancers at the time of participant recruitment (i.e., breast, prostate, bladder, uterine, skin melanoma, colorectal, kidney, non–Hodgkin lymphoma, ovarian, and lung cancer); diagnosed with a local, regional, or distant Surveillance, Epidemiology, and End Results (SEER) summary stage; diagnosed between January 2000 and September 2003, and fluent in English or Spanish. Minority race/ethnicities, survivors below age 55, and survivors of cancers with moderate or low survival (e.g., kidney, lung cancer) were oversampled. The Institutional Review Board of Emory University approved SCS-I, with additional approvals for each state. Additional information about the methodology of SCS-I is available elsewhere.[95]

Smoking status and history (e.g., age at quit) was assessed only at Wave 3. Participants were asked whether they had smoked at least 100 cigarettes in their lifetime, and if so, whether they currently smoked every day or some days. Those who were not current smokers but had smoked at least 100 cigarettes were asked their age at quitting. Of the 2,752 cancer survivors who answered smoking questions at Wave 3, 246 indicated they were current smokers, and an additional 95 indicated that they had quit after they were diagnosed with cancer. These 341 cancer survivors comprise the analytic sample for this study. Sample sizes for each analysis were between 297 and 323, as cases with missing data on key predictors were dropped.

Measures

Length of time between cancer diagnosis and quitting—outcome variable:

The difference in years between participants' age at diagnosis, and their age when they subsequently quit was calculated by subtracting a survivor's age when they quit smoking from their age at diagnosis (reported at Wave 1). Values ranged from 1-10 years. Current smokers' completion of the Wave 3 assessment counted as their "event," although they had not yet quit at that assessment because the survival time in time-to-event analysis is at least as long as the period that each participant was followed (i.e., these data are right-censored).[96] Thus, for current smokers, survival time was coded as the survivor's age in years at Wave 3 minus the survivor's age at diagnosis. We also created a separate variable representing censorship status, as is typically done in time-to-event analysis,[96] to differentiate current smokers who were diagnosed 10 years ago from survivors who quit 10 years after diagnosis.

Psychological Distress—predictor variable:

Psychological distress was assessed in Wave 1 using the 37-item Profile of Mood States-Short Form scale (POMS-SF).[97] For each item, respondents indicated on a 5-point scale from 0 "not at all" to 4 "extremely" how much they had been feeling each mood (e.g., uneasy, grouchy, nervous, annoyed) during the past two weeks. Scores were derived for total negative mood and for six factor-based subscales. The following six subscales with Cronbach's α levels ranged from .85 to .95 include: Depression-Dejection; Vigor-Activity; Confusion-Bewilderment; Tension-Anxiety; Anger-Hostility; Fatigue-Inertia. We obtained the total score by summing the subscale Depression-Dejection, Confusion-Bewilderment, Tension-Anxiety, Anger-Hostility, and Fatigue-Inertia scores minus the Vigor-Activity scores. Higher total scores indicate higher psychological distress with scores ranging from -24 to 111. Scores were dichotomized based on a

median split as done in previous research[98] to aid in the interpretation of findings: scores at or below the median value of 10 were considered low psychological distress and scores above the median were considered high psychological distress.

Health-Related Quality of Life—predictor variable:

HRQOL was assessed in Wave 1 using the Medical Outcomes Study Short Form-36 (MOS SF-36).[99] MOS SF-36 is a 36-item, commonly used self-report tool that consists of eight subscales including physical functioning (e.g., bathing or dressing yourself), role-physical (e.g., as a result of physical health, had difficulty performing work), bodily pain, general health (e.g., my health is excellent), vitality (e.g., have a lot of energy), social functioning (e.g., frequency health problems interfered with social activities), role-emotional (e.g., as a result of emotional problems, extent accomplished less than you would like), and mental health (e.g., felt calm and peaceful). Cronbach's α levels for subscales ranged from .85-.91. The MOS SF-36 is scored on two component summary scales for physical (PCS) and mental (MCS) health, which are both summed over all eight subscales (items related to physical health are negatively weighted in the MCS and items related to mental health are negatively weighted in the PCS), from which we derived two dichotomous variables for physical and mental HRQOL. The range was 13 to 68 for the PCS and 11 to 66 for the MCS. For each, survivors who scored 1 standard deviation at or below a national normalized mean (≤ 40) were considered to have low HRQOL and those who scored above that value were considered to have high HRQOL; this categorization of the MCS and PCS has previously been used in the literature.[100]

Perceived Social Support—predictor variable:

Perceived social support was assessed in Wave 1 with the Multidimensional Scale of Perceived Social Support (MSPSS).[101] This 12-item self-report inventory measures perceived

adequacy of social support from significant others, family, and friends on a 7-point Likert-type scale ranging from 1 "very strongly disagree" to 7 "very strongly agree." Example items include, "There is a special person with whom I share my joys and sorrows;" "My family really tries to help me;" and "I can talk about my problems with my friends" Scores from all items were summed to create a total score, where higher scores indicate higher perceived social support; scores ranged from 12 to 84 (Cronbach's α =.99). Scores were dichotomized for analyses using median split as done in a previous study[102]: scores at or below the median score of 5.83 were considered low social support and score above the median were considered high social support.

Tobacco-related cancer diagnosis—control variable:

Diagnosis of a tobacco-related cancer was recorded through the cancer registry data and confirmed by self-report in the Wave 1 survey. We created a dichotomous tobacco-related cancer variable based on the type(s) of cancer the participants reported having, using the classifications in the International Agency for Research on Cancer (IARC) guidelines,[103] which has been used in previous studies.[47,49] IARC guidelines consider tobacco-related cancers to include colorectal, bladder, kidney, and lung cancers, and non-tobacco-related cancers to include breast, prostate, uterine, skin melanoma, non–Hodgkin lymphoma, and ovarian cancers.

Comorbid conditions—control variable:

We also included number of comorbid conditions as a covariate in our models. In Wave 1, participants indicated "yes" or "no" if they had been treated in the past five years for each of the following conditions: Alzheimer's disease, Crohns disease, diabetes, high blood pressure, heart attack, other heart conditions, stroke, circulatory problems, arthritis, asthma, osteoporosis, enlarged prostate, frequent infections. We summed the number of comorbid conditions to create a comorbidity index that ranged from 0 to 13.

Analytic Strategy

We used time-to-event analysis—also known as survival analysis—to test our hypotheses. First, we ran separate Cox regression models regressing quitting smoking on each psychosocial factor, both without control variables (Model 1) and with control variables (Model 2). We obtained a Hazard Ratio (HR) to indicate whether survivors with poorer psychosocial wellbeing were less likely to quit after diagnosis compared to those with better psychosocial wellbeing. We added an interaction with time for each psychosocial factor to assess if the data violated the proportional hazards assumption.[96] We compared Kaplan Meier survival curves and their corresponding Log Rank p-value for each dichotomous Wave 1 psychosocial factor. The Kaplan Meier curves for each model illustrate how the probability of quitting after diagnosis differs based on the two levels of each predictor over time. To provide further insight into results, we conducted exploratory analyses to examine how any significant associations we observed differed by type of cancer (tobacco-related or non-tobacco-related). We incorporated the discrete nature of the data into the analyses using the "ties=exact" statement in SAS. Survey weights were incorporated for Wave 3 that adjusted for oversampled populations in the descriptive analyses but not in inferential analyses. We used SAS version 9.4 to conduct all analyses two-tailed with a critical alpha of .05.

Results

Table 1 describes the characteristics of the sample. The majority of the sample were current smokers (68.2%), survivors of non-tobacco-related cancers (76%), female (53.4%), non-Hispanic-White (88%), and had completed at least some college (60.7%). The mean age of the sample was 59.5 years (SE: 1.0).

In unadjusted analyses (Table 2-Model 1), none of the psychosocial factors of interest were significantly associated with quitting smoking (Table 2). In adjusted analyses (Model 2), however, physical HRQOL was significantly associated with quitting. Those with high physical HRQOL at baseline were almost twice as likely to quit smoking within 10 years of diagnosis compared to those with low physical HRQOL, after adjusting for cancer type and number of comorbid conditions (HR = 1.96; 95% CI: 1.11-3.46; p=.02). These data did not violate the proportional hazard assumption. The unadjusted Kaplan Meier curve (Figure 3) illustrates that for those with high physical HRQOL, the increase in the probability of quitting started at two years after diagnosis and steadily increased over time. In those with poor physical HRQOL, the most noticeable initial increase in quitting occurred at six years from diagnosis. The unadjusted Kaplan Meier curves for psychological distress, perceived social support, and mental HRQOL (Figures 1-2, 4) all suggest that the probability of quitting smoking gradually increases for both low and high categories of groups over time, especially after four years from diagnosis.

We plotted a survival curve for physical HRQOL on quitting, stratifying by cancer type, to further explore how the probability of how quitting changed over time for each level of physical HRQOL and cancer type (Figure 5). At each year after diagnosis within the timeframe of the study, survivors of tobacco-related cancers with high physical HRQOL were more likely to quit smoking than any other group. In all years except years 5-7 after diagnosis, survivors of tobacco-related cancers with low physical HRQOL were the least likely group to quit smoking. Additionally, the time at which the first increase in quitting occurred varied by both physical HRQOL and cancer type. The initial increase in quitting occurred two years post-diagnosis for survivors of both types of cancers who had high physical HRQOL. Among those with low

physical HRQOL, increases in quitting began 4 and 7 years post-diagnosis for tobacco-related and non-tobacco-related cancer survivors, respectively.

Discussion

Of the four psychosocial variables that we examined, only physical HRQOL was significantly associated with smoking cessation and the time at which cessation occurred in the sample of cancer survivors. Specifically, we found that cancer survivors with low physical HRQOL one year after diagnosis were less likely to successfully quit smoking within ten years of diagnosis than survivors with high physical HRQOL, when controlling for cancer type and number of comorbid conditions. Survivors with low physical HRQOL also took longer to quit than survivors with high physical HRQOL. The first noticeable increase in the probability of quitting occurred at two years after diagnosis in survivors with high physical HRQOL compared to year six in survivors with low physical HRQOL. Survivors of tobacco-related cancer with high physical HRQOL were the most likely group to quit smoking, while survivors of tobacco-related cancer with low physical HRQOL were the least likely group to quit.

These results suggest that cancer survivors with low physical HRQOL might use cigarettes as a way to cope with their pain and poor physical functioning. However, although we observed that low physical HRQOL one year after diagnosis is associated with lower quit rates over time, our research cannot make causal assertions about the nature of this association. It is possible that higher nicotine addiction and higher cigarette consumption both worsen physical HRQOL and make quitting more difficult. Research that accounts for these factors, as well as qualitative research studies with survivors with low physical HRQOL, are needed to better understand the unique barriers to quitting these survivors face.

Our results suggest that if future research corroborates our findings on HRQOL and cessation, it might be worthwhile for oncology clinicians to assess physical HRQOL in their patients and provide more intensive long-term cessation resources to smokers with poor physical HRQOL, who might have a particularly difficult time quitting smoking. Smoking cessation interventions that include strategies to mitigate physical symptoms in those with poor physical HRQOL (e.g., by incorporating acupuncture or occupational therapy to combat persistent fatigue and pain) deserve consideration in research and practice.

More research is also needed to understand reasons why survivors with low physical HRQOL may take longer to quit than survivors with high physical HRQOL. Assessing various predictors and risks for smoking cessation several years after diagnosis might inform interventions to shrink the time window that it takes survivors with low physical HRQOL to quit.

In our exploratory analyses, we found that survivors of tobacco-related cancers with low physical HRQOL were the least likely group to quit smoking, though the reasons for this are unclear. Research is needed to examine the specific barriers to quitting experienced by survivors of tobacco-related cancer with lower physical HRQOL so that these survivors can be appropriately targeted in smoking cessation interventions.

Our hypotheses on psychological distress, perceived social support, and mental HRQOL were not supported: we did not find a significant association between those psychosocial variables and quitting nor did it appear that those factors influenced the length of time until quitting in this sample. Although studies with the general population suggest each of these may be important predictors of smoking,[40-42] they may change significantly over time in cancer survivors, so that any single observation of these factors may not sufficiently predict cessation. A systematic review of quality of life outcomes of long-term survivors of various cancer types

found that overall HRQOL increases over time after cancer diagnosis, although issues with physical HRQOL (e.g., pain, fatigue) can persist for years.[44] Mental HRQOL at the time of diagnosis might therefore be related to quitting smoking in the first year of diagnosis, but the effects might taper off after one year as cancer survivors return to a more normal lifestyle. Alternatively, the effect sizes of these psychosocial factors on quitting may have been too small to detect in our sample. These analyses should be replicated in studies with larger sample sizes, and more observations of both predictors and smoking over time.

Even among survivors of tobacco-related cancers with high physical HRQOL—the group most likely to quit smoking— the majority (56.5%) of respondents were still smoking 10 years following diagnosis. Exploring other predictors of quitting smoking in long-term survivors will be important to design more comprehensive interventions. Levels of anxiety or depressive symptoms, as well as specific social support for quitting have been linked to smoking outcomes in cancer survivors in past studies, and deserve more consideration in future research.[8,71,104,105]

There are several strengths to this study. First, data came from a longitudinal national study of long-term (> 5 years) cancer survivors, which allowed us to use time-to-event analysis to identify not just who was less likely to quit smoking but also how much longer it took certain groups to quit, which has implications for when to intervene. Second, this study included survivors of various cancer types, which allowed us to examine how the probability of quitting smoking changed based on levels of each psychosocial factor and cancer type. This analysis further identified populations (e.g., survivors of tobacco-related cancer with low physical HRQOL) that might need more intensive cessation resources over time.

There are limitations of this study that are important to consider. The variable time since quitting was imprecisely measured because age at quitting was measured in years. Using years as

the unit of measurement might not reflect an accurate time of when survivors quit smoking. The yearly hazard ratio of quitting smoking, however, has been used in another time-to-event analysis study[106] and we incorporated the discrete nature of the data into the analyses. More precise measures of the length of time until quitting in days or months, rather than in years, may help us better understand the best windows of opportunity for intervention. Second, smoking status was assessed retrospectively at a single time point. It would be informative for future studies to conduct these analyses with prospective data that contain multiple assessments of both psychosocial factors and smoking status over time to improve our understanding of this association. Last, this analysis relies on data from longtime cancer survivors. The generalizability of any findings from this work, however, has to be understood as applicable only to individuals who do survive 7-10 years post diagnosis. In our sample, participants in Wave 1 with the following characteristics were more likely to remain in Wave 3: survivors of non-tobacco-related cancer, those with lower comorbid conditions at Wave 1, lower psychological distress, higher mental and physical HRQOL, and higher perceived social support. The smoking rate was low in the Wave 3 sample (7.8%); if the people lost to follow-up were also particularly unlikely to quit smoking and were perhaps heavier smokers and had worse psychosocial outcomes, had we included them in the analytic sample, our results might have been different.

Conclusions and Implications

Survivors in this sample with low physical HRQOL were both less likely to quit and took several more years to quit than survivors with high physical HRQOL. These results suggest that should our findings be corroborated in future research, we recommend that smoking cessation programs explicitly provide cancer survivors with low physical HRQOL, and especially survivors of tobacco-related cancers, with intensive long-term smoking cessation interventions

with multiple check-in points after smoking relapses. Smoking cessation interventions might need to also include strategies to help cancer survivors with low physical HRQOL manage their symptoms (e.g., strategies that reduce pain and fatigue). Recognizing the importance of physical HRQOL as a predictor of smoking cessation and the amount of time it takes to quit could be an important step in creating more effective cessation interventions designed specifically for cancer survivors throughout the cancer continuum.

Table 3.1: Characteristics of the Sample
(n =341)

Characteristic	N	%/Mean/SE[a]	Missing N (%)
Smoking Status[b]			0 (0)
Current smoker	246	68.2	
Quit after diagnosis	95	32.8	
Cancer Type			1 (0.3)
Tobacco-related	111	24.0	
Non-tobacco-related	229	76.0	
Gender			0 (0)
Female	191	53.4	
Male	150	46.6	
Race			2 (0.6)
Non-Hispanic White	300	88.0	
Non-Hispanic Black	24	10.0	
Hispanic	10	1.4	
Other	5	0.6	
Completed Education			3 (0.9)
Less than HS	36	14.4	
HS graduate	101	24.2	
Some college	117	42.7	
College degree or more	81	18.0	
Age at Wave 1	341	59.5 (1.0)	0 (0)
Number of Comorbid Conditions at Wave 1	338	0.9 (0.1)	3 (0.8)
Time Until Quit Smoking	95	Median: 4.6 (0.8)	0 (0)
Psychological Distress	297	17.1 (1.5)	44 (12.9)
HRQOL			30 (8.8)
PCS	311	47.7 (0.6)	
MCS	311	46.3 (0.7)	
Perceived Social Support	323	5.6 (0.1)	18 (5.3)

a. Percentages and means/medians/SE are weighted.
b. Smoking status assessed only at Wave 3

Table 3.2: Cox Proportional Hazard Models

	Model 1			Model 2		
Characteristic	**Total**	**Hazard Ratio 95% CI**	**P-Value**	**Total**	**Hazard Ratio 95% CI**	**P-Value**
Psychological Distress	297	1.22 (0.78-1.91)	.28	293	1.25 (0.80-1.96)	.33
Cancer Type		---	---		1.73 (1.10-2.70)*	.02
Comorbid Conditions		---	---		1.08 (0.86-1.35)	.52
Perceived Social Support	323	1.14 (0.76-1.73)	.53	319	1.16 (0.77-1.77)	.48
Cancer Type		---	---		1.50 (0.98-2.28)	.06
Comorbid Conditions		---	---		1.16 (0.96-1.40)	.13
Physical HRQOL	311	1.54 (0.90-2.66)	.12	308	1.96 (1.11-3.46)*	.02
Cancer Type		---	---		1.54 (1.00-2.37)	.05
Comorbid Conditions		---	---		1.29 (1.04-1.59)*	.02
Mental HRQOL	311	1.24 (0.78-1.97)	.37	308	1.32 (0.82-2.11)	.26
Cancer Type		---	---		1.44 (0.94-2.21)	.10
Comorbid Conditions		---	---		1.21 (0.98-1.49)	.07

Notes: Reference categories: Psychological distress (high); Cancer type (non-tobacco-related); Perceived social support (low); Physical HRQOL (low); Mental HRQOL (low).
Model 1: No control variables
Model 2: Controls for cancer type and number of comorbid conditions; AICs were smaller in Model 2
* Indicates $p < .05$

Figure 3.1: Unadjusted Kaplan Meier Survival Curve for Psychological Distress (*n* = 297)

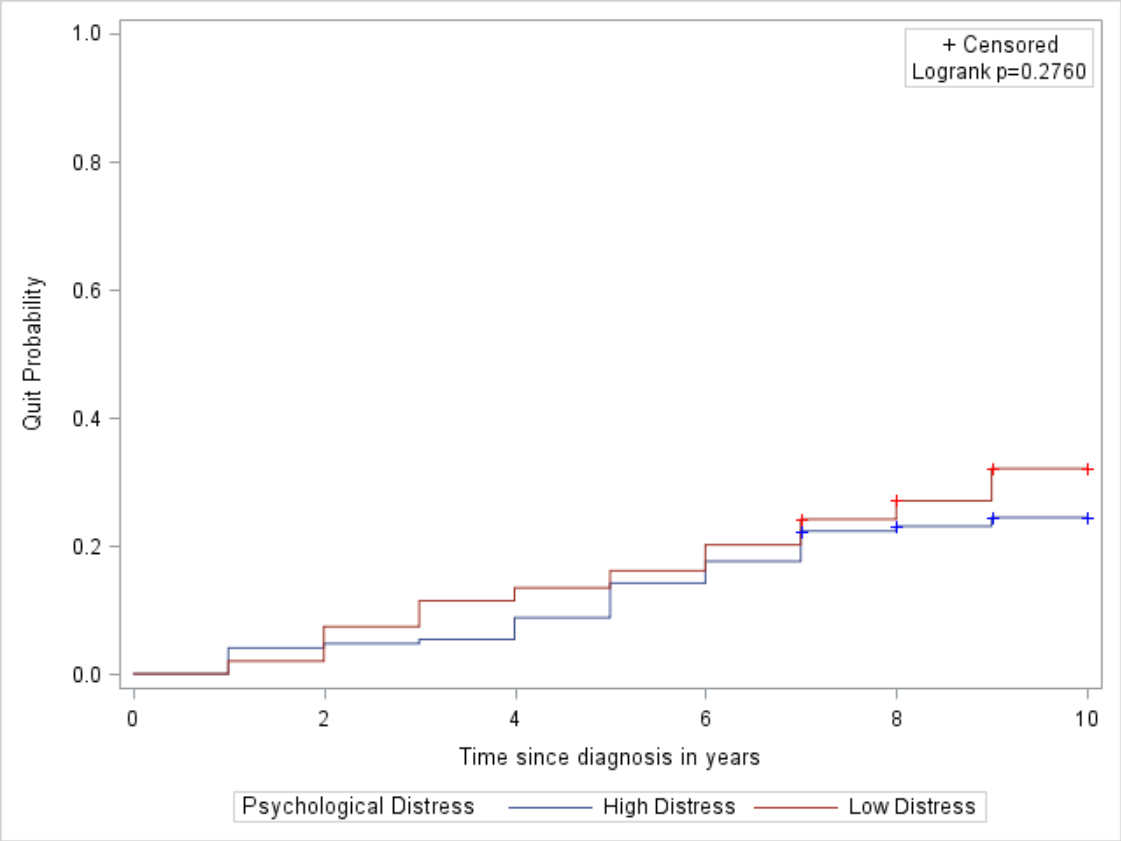


Figure 3.2: Unadjusted Kaplan Meier Survival Curve for Perceived Social Support (*n* = 323)

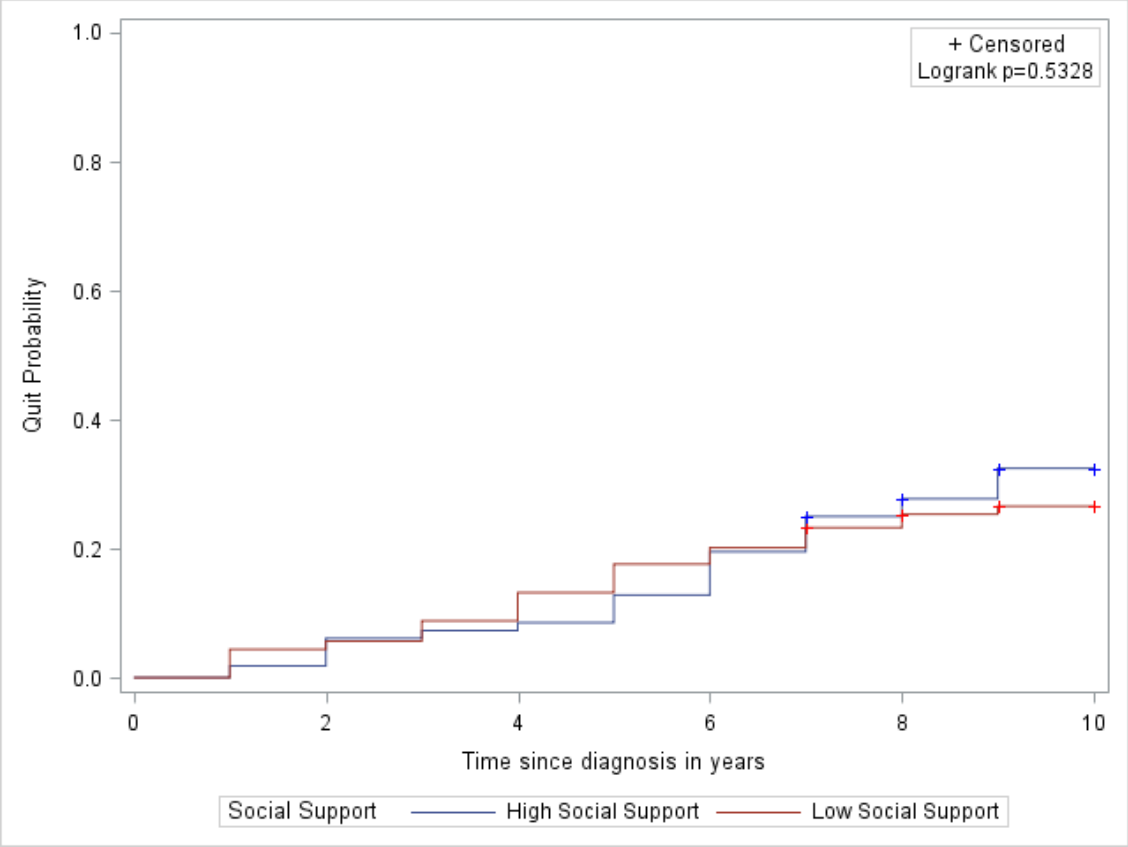


Figure 3.3: Unadjusted Kaplan Meier Survival Curve for Physical HRQOL
(*n* = 311)

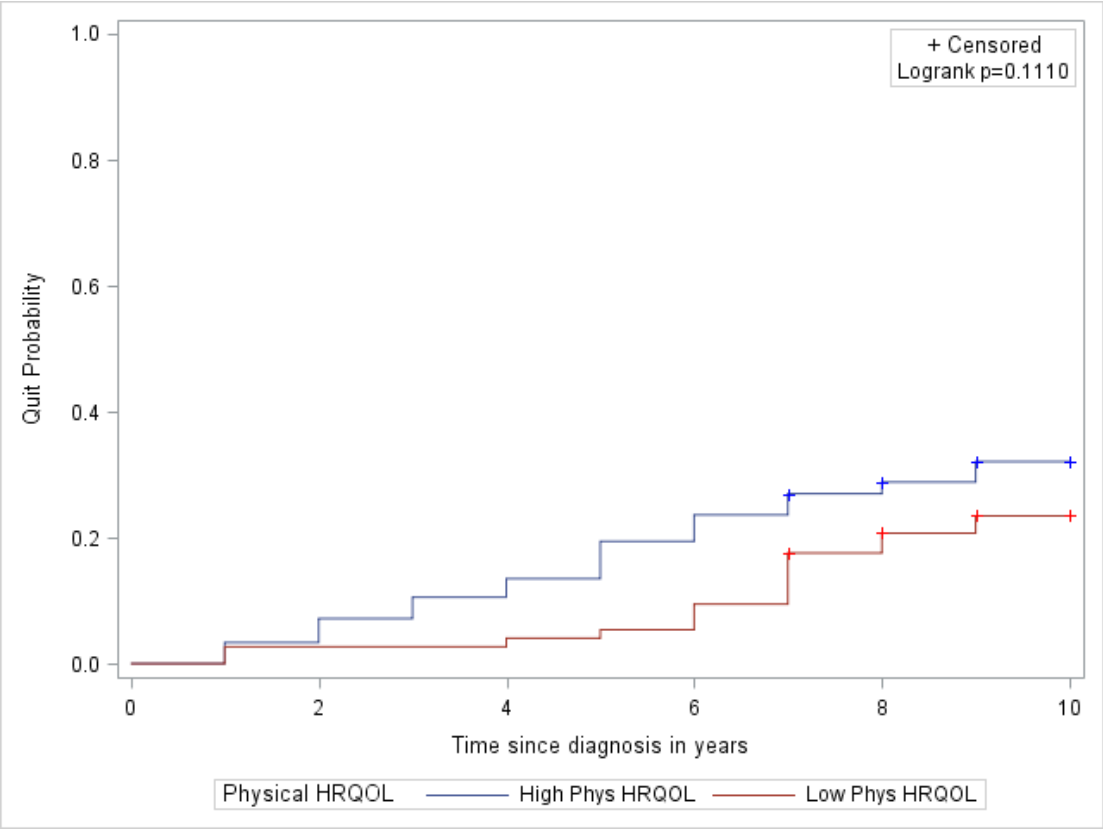


Figure 3.4: Unadjusted Kaplan Meier Survival Curve for Mental HRQOL
(*n* = 311)

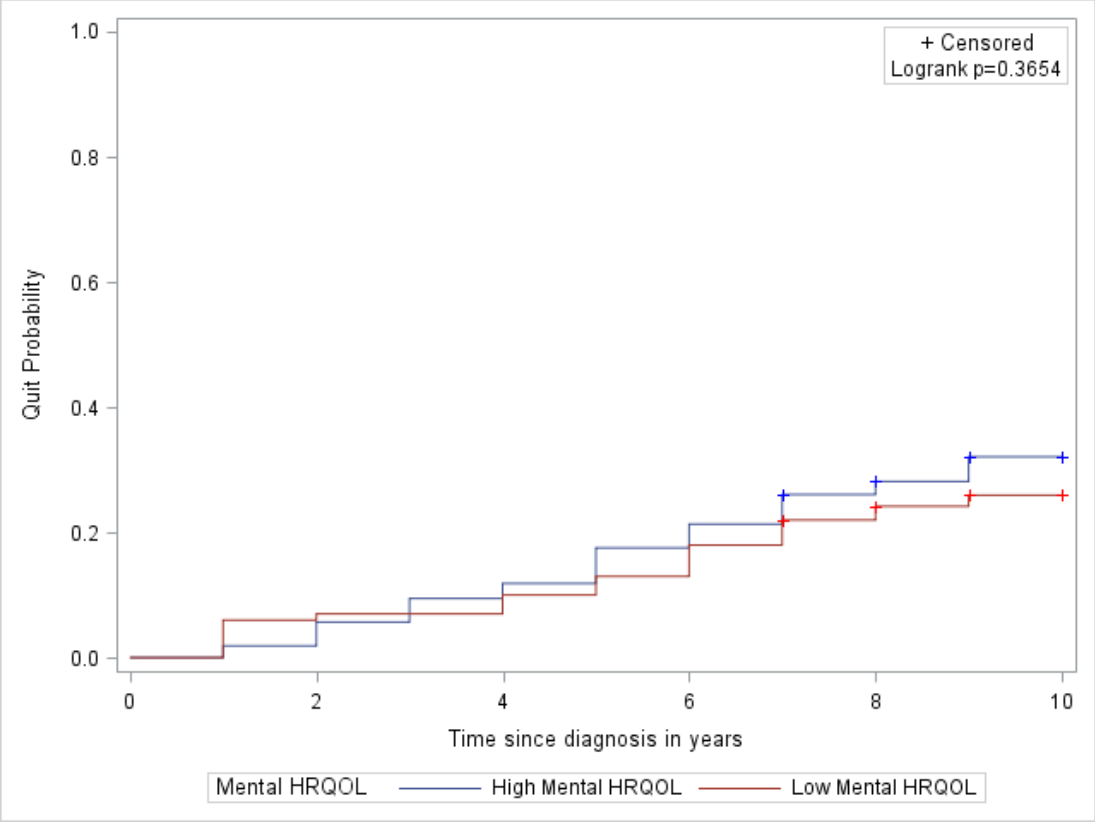
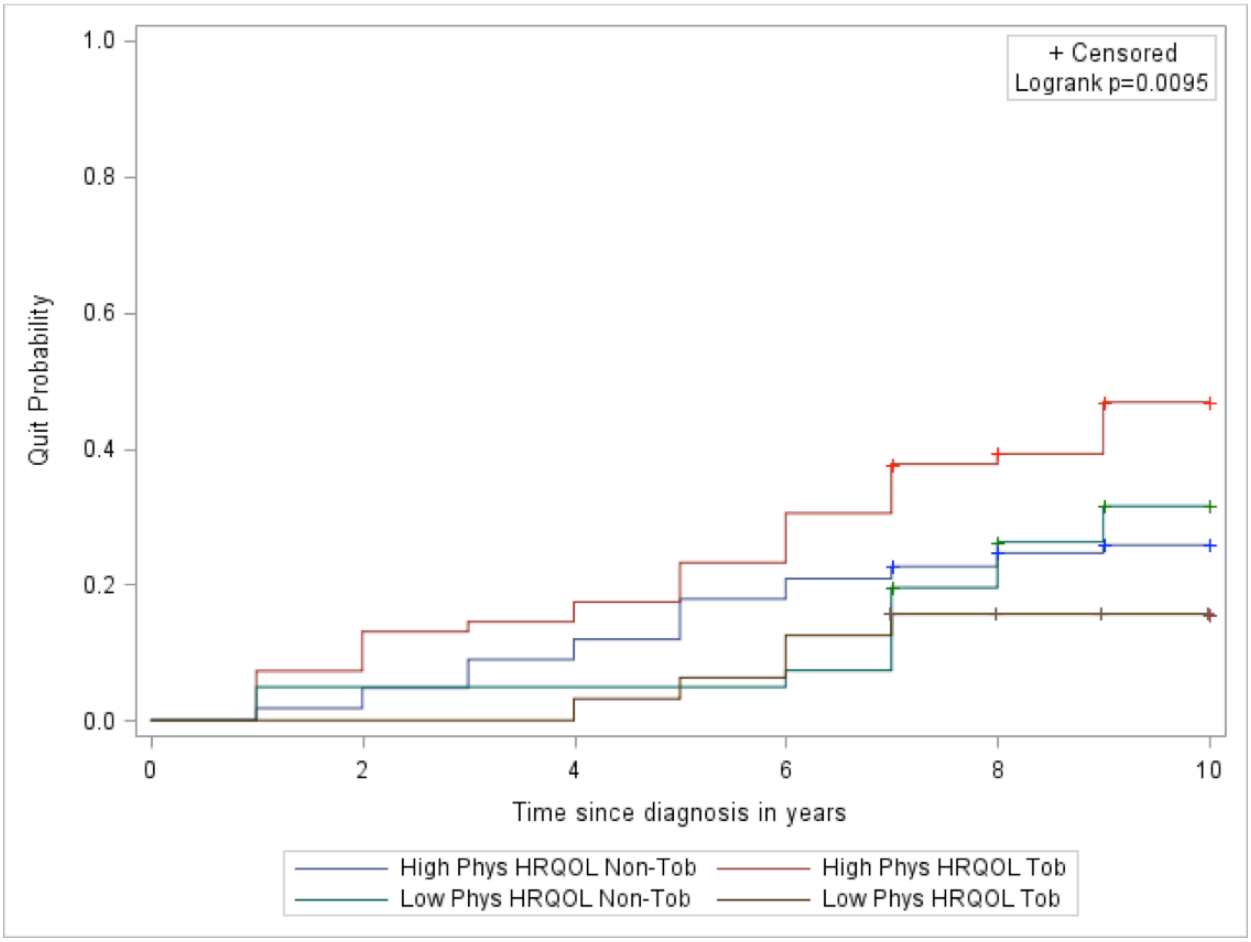


Figure 3.5: Survival Curve for Physical HRQOL Adjusted for Cancer Type
(*n* = 311)



CHAPTER 4: MANUSCRIPT 2-
DIAGNOSIS OF TOBACCO-RELATED CANCER AND PERCEIVED SEVERITY OF HEALTH PROBLEMS FROM SMOKING IN CANCER SURVIVORS

Purpose. Cancer survivors diagnosed with tobacco-related cancers (e.g., lung, head and neck) quit smoking at higher rates than those diagnosed with non-tobacco-related cancers (e.g., breast, prostate). Survivors of tobacco-related cancers—who are more likely to attribute their cancer to their tobacco use—might have higher perceived severity of health problems from smoking than survivors of non-tobacco-related cancers, which might in turn influence cessation. Understanding differences in smoking beliefs between the two groups could help clinicians target smoking cessation interventions. **Methods.** We conducted linear regression analyses using Wave 1 of the Population Assessment of Tobacco Health (PATH) study to examine differences in perceived severity of health problems from smoking between smokers who were survivors of tobacco vs. non-tobacco-related cancers. We then explored whether this difference varied by time since diagnosis. **Results.** We found that survivors of tobacco-related cancers reported higher perceived severity of health problems from smoking than other survivors ($\beta = .25$, $p = .04$) and this relationship was the same for recently diagnosed and long-term survivors. **Conclusions**. Our findings suggest that differences in quit rates between survivors of tobacco and non-tobacco-related cancers could at least in part be attributed to differences in perceived severity of health problems from smoking that persist for years after diagnosis.

Introduction

Smoking after a cancer diagnosis is associated with lower survival,[2,4] higher rates of recurrent disease,[5] more secondary tumors,[19-23] decreased efficacy of cancer treatment,[3] increased treatment-related complications and symptom burden, [6,24,25] and lower quality of life (QOL).[27-30] Smoking prevalence rates among cancer survivors after diagnosis range widely as a function of cancer type, with estimates ranging anywhere from 7-51%.[1,8,12,13] Survivors of tobacco-related cancers (e.g., cervical, bladder, and lung cancer) report the highest rates of smoking after diagnosis (ranging from 27%-51%) in part because they were more likely to smoke before diagnosis.[1,8,12,13] One study that aggregated smoking status across survivors of various tobacco-related cancers found that 51% continued to smoke after a cancer diagnosis.[8] Conversely, survivors of non-tobacco-related cancers such as prostate and breast cancer, tend to report low rates of smoking after diagnosis (7.7% and 11.9%, respectively).[1] Although initial smoking rates are higher among those diagnosed with a tobacco-related cancer, several studies have found that smokers who are diagnosed with tobacco-related cancers quit smoking at higher rates than smokers diagnosed with other cancer types.[47,49] These findings, however, are not universal. A large study found similar quit rates post-diagnosis for survivors of various cancer types, although lung and head and neck cancers were excluded from those analyses.[107] There is little investigation on mechanisms that might explain the difference in quit rates between survivors of tobacco and non-tobacco-related cancers.

The Health Belief Model[66] and the Cognitive-Social Health Information Processing model (C-SHIP)[68,69] posit that high perceived severity of health problems from smoking (e.g., believing that smoking is harmful to health) leads to higher intentions to quit smoking, and ultimately higher rates of smoking cessation. In a study by Westmaas et al., the odds of quitting

smoking after a cancer diagnosis were higher for those with higher perceived severity of smoking-related health problems.[70] Another study that identified correlates of continued smoking after diagnosis in head, neck, and lung cancer patients found that those who continued to smoke versus those who quit smoking reported lower perceptions of risk of continued smoking (i.e., awareness of adverse health effects of continued smoking such as an increased risk in cancer recurrence).[51] This evidence indicates that the perceived severity of health problems from smoking is an important construct related to smoking cessation outcomes in cancer survivors.

The perceived severity of health problems from smoking might help explain the relationship between the diagnosis of tobacco-related cancer and smoking cessation. Survivors of tobacco-related cancers might have higher perceived severity of health problems from smoking than survivors of non-tobacco-related cancers if they are more likely to attribute their cancer to their tobacco use. In one study, lung cancer patients who smoked were more likely than breast and prostate cancer patients to believe their smoking behavior contributed to their cancer.[74] In a qualitative study of lung, liver, stomach, nasopharynx, or colorectal cancer survivors who currently smoke, many of the survivors who were diagnosed with cancers other than lung cancer, reported that they were unaware of the association between their cancer diagnosis and smoking; some thought smoking is only associated with lung cancer.[72] Additionally, because of the well-known link between smoking and tobacco-related cancers,[8,108] many survivors of tobacco-related cancer might be advised by their loved ones and clinicians to quit, which in turn might promote higher perceived severity of health problems from smoking. Survivors of non-tobacco related cancers are perhaps not as frequently advised to quit. In one study of long-term survivors of mostly breast, prostate, and gastric cancers who smoked at diagnosis found that almost 60% had not been advised to quit smoking by their clinicians.[33] In contrast, lung and head and neck cancer

patients might be exposed to more recommendations to quit: a large study of lung cancer physicians found that 81% advise their patients who smoke to quit at their initial patient visit.[109]

To our knowledge, there are no published studies that explore if survivors of tobacco-related cancers report higher perceived severity of health problems from smoking than survivors of non-tobacco-related cancers. If there are indeed differences in perceived severity of health problems from smoking between the two groups of survivors, then this is a construct that might help to inform cessation intervention efforts with cancer survivors, particularly for survivors of non-tobacco-related cancers, which is a group that tends to quit at lower rates. Further, if survivors of tobacco-related cancers have higher perceived severity of smoking than survivors of non-tobacco-related cancers, it is possible that this difference is particularly pronounced immediately following diagnosis when health and mortality are most salient. Researchers have argued that the time directly after diagnosis can serve as a "teachable moment" to cancer survivors who are likely most motivated to quit at this time.[94,107,110,111] As time goes on after diagnosis, those who survive and continue to smoke might perceive fewer risks about smoking if they continue to survive and not develop comorbidities years after their diagnosis while continuing to smoke. Thus, if the difference in perceived severity between the two groups of survivors is small several years after diagnosis, then it would be crucial to target survivors of non-tobacco related cancers very early on in the cancer continuum when their perceived severity is significantly lower than that of survivors of tobacco-related cancers.

In the current study, we explore differences in perceived severity of health problems from smoking between survivors of tobacco and non-tobacco-related cancers in a large national sample that includes survivors of various cancer types. To identify the optimal time to provide

smoking cessation interventions to each group, we also test if this relationship significantly differs as a function of time since diagnosis. We hypothesize:

1.) Survivors of tobacco-related cancers will report greater perceived severity of health problems caused by smoking than survivors of non-tobacco-related cancers;

2.) The difference in perceived severity of health problems from smoking between survivors of tobacco-related and non-tobacco-related cancer will be largest in survivors who have been diagnosed within two years. For those cancer survivors who experience survival beyond the initial active treatment phase (>2 years from diagnosis), both groups will have similar low levels of perceived severity.

Methods

Data Source and Samples

We tested our hypotheses using data from Wave 1 of the Population Assessment of Tobacco Health (PATH) study, a U.S. national longitudinal survey of tobacco users and non-users, funded by the National Institute of Health's National Institute on Drug Abuse, and through the Food and Drug Administration (FDA) Center for Tobacco Products.[112] Data were collected between 2013-2014 by audio computer-assisted self-interviewing (ACASI) and computer-assisted personal interviewing (CAPI) questionnaires. The PATH study over-sampled tobacco users, young adults aged 18-24, and African Americans and used a stratified probability sampling design of 156 geographical primary sampling units (PSUs) with a final sample of 32,320 adults 18 years and older. The PATH sample includes 433 cancer survivors who currently smoke every day or some days; we had complete data for our analyses for 409 (95%) of those survivors, which we used as our primary analytic dataset. The Institutional Review Board at the

University of North Carolina at Chapel Hill exempted the secondary analyses of PATH data as not human subjects research.

Measures

Diagnosis of Tobacco-Related Cancer:

Type of cancer diagnosis was recorded through self-report in Wave 1. We created a dichotomous tobacco-related cancer variable based on the type(s) of cancer the participants reported having, using the classifications in the International Agency for Research on Cancer (IARC) guidelines [103], which has been used in previous studies.[17,47,49] IARC guidelines consider tobacco-related cancers to include the following cancers: bladder, cervix, colon, esophagus, kidney, larynx/windpipe, liver, lung, mouth/tongue/lip, pancreas, stomach, throat, and uterus. We classified non-tobacco-related cancers as cancers of the blood, brain, breast, gallbladder, nervous system, prostate, rectum, ovary, soft tissue (muscle or fat), testis, thyroid, and lymphoma/Hodgkin disease and melanoma. Survivors of non-melanoma skin or "other" cancers were not included in these analyses because they are not generally included in studies of cancer survivors.

Perceived severity of health problems.

Perceived severity of health problems from smoking was assessed with two items, both rated on four-point scales: "To what extent, if at all, has using tobacco products damaged your health?" (rated from "not at all" to "a lot") and "To what extent, if at all, are you worried that using tobacco products will damage your health in the future?" (rated from "not at all worried" to "very worried"). Scores were averaged to create a composite score that ranges from 1-4, with higher scores indicating higher perceived severity of health problems from smoking ($r = .53$).

Length of time since diagnosis.

Survivors in the PATH study reported their current age as well as their age at the time of their diagnosis. Time since diagnosis was created by subtracting current age from age at diagnosis. Responses were dichotomized into: 1) diagnosed within two years and 2) diagnosed over two years ago. We chose the cut-off of two years after diagnosis because most primary treatments of cancer are likely completed within this time frame. The time after two years from diagnosis likely marks a reduced frequency in regular interactions with oncology clinicians.

Covariates.

In addition to age in years, demographic variables included level of education (0=less than high school education and 1=high school education and above), race/ethnicity (1=non-Hispanic White or 0=other race/ethnicity), and gender (0=female or 1=male) were included in the analyses as they have been previously shown to relate to smoking outcomes in the general population and in cancer survivors.[11,35,47,49]

Analytic Strategy

We first used logistic regression to confirm that previous associations between cancer type and cessation existed in the PATH data, using data from all survivors with a smoking history (n = 1,235). The focus of this study, however, was to examine differences in beliefs about the harms of smoking by cancer type among current smokers only. Using the primary sample described above, we examined the relationship between diagnosis of tobacco-related cancer and perceived severity of health problems from smoking using linear regression. In Model 1, we examined whether a diagnosis of tobacco-related cancer, controlling for age, race, education, sex, and length of time since diagnosis was significantly related to perceived severity of health problems from smoking. In Model 2, we added the interaction term of cancer diagnosis type ×

length of time since diagnosis. We used SAS version 9.3 to conduct all analyses, which were two-tailed with a critical alpha of .05. We incorporated survey weights provided by the creators of the PATH data in all analyses, to compensate for variable probabilities of selection, differential nonresponse rates, and possible deficiencies in the sampling frame (e.g., under coverage of certain population groups).

Results

Table 1 describes characteristics of the sample in our study. A majority of survivors were diagnosed with non-tobacco-related cancers (58.1%), were diagnosed more than two years prior to survey (80.5%), and were female (64.3%), non-Hispanic White (82.5%), with at least a high school education (69.4%). The mean age of the sample was 54 (SE = 0.7). The mean perceived severity of health problems was 2.6 (SE = 0.1). In χ^2 analyses, there was a significant difference between the two groups of survivors in education ($p < .001$): there was a higher percentage of less than high school-educated participants in the sample of survivors of tobacco-related cancers compared to survivors of non-tobacco-related cancers (37.7% versus 25.5%, respectively). There were no other significant differences in characteristics between the two groups.

As in past studies of quit rates between the two groups of survivors, PATH survivors of tobacco-related cancer were significantly more likely to quit smoking after diagnosis (14.3% quit) than survivors of non-tobacco-related cancer (11.9% quit), after controlling for race, education, gender, and age (OR: 2.44; 95% CI: 1.49-3.99; p<.0001, results not shown).

Table 2 displays the results from the linear regression model that tested the relationship between diagnosis of tobacco-related cancer and perceived severity of health problems from smoking. Our main effect hypothesis (Model 1) was supported: those diagnosed with tobacco related cancers reported higher perceived severity of health problems from smoking compared to

those diagnosed with non-tobacco-related cancers (β = .25; 95% CI: .01-.49; *p* = .04). Contrary to our interaction hypothesis, the relationship between tobacco-related cancer diagnosis and perceived severity of health problems from smoking did not vary by length of time since diagnosis (interaction term β = .09; 95% CI: -.06-.52; *p* = .76). In other words, the relationship between diagnosis of tobacco-related cancer and perceived severity was the same for recently diagnosed and for long-term survivors (Model 2).

Discussion

Our study found that survivors of tobacco-related cancer reported higher perceived severity of health problems from smoking than survivors of non-tobacco-related cancer and that this relationship was the same for short-term and long-term survivors. This finding highlights: 1) that the belief about the harms of smoking is a potentially important factor that could explain why survivors of tobacco-related cancer quit at higher rates than survivors of non-tobacco-related cancer and 2) that there might not be just one "teachable moment" in changing beliefs about the harms of smoking because differences in perceived severity between the two groups persisted for years after diagnosis. Clinicians who continue to discuss the harms of tobacco use after cancer diagnosis throughout ongoing care (e.g., through motivational interviewing techniques)— particularly with their patients with non-tobacco-related cancers, could contribute to increased intentions to quit, and ultimately smoking cessation among some patients. Future research with longitudinal data with multiple assessments of perceived severity and smoking status over time should investigate the extent that the perceived severity of the harms of smoking mediates the relationship between diagnosis of tobacco-related cancer and smoking cessation.

One potential explanation for differences in beliefs by cancer type that we observed is that survivors of tobacco-related cancer receive more provider advice to quit and social pressure

from friends and family, each of which might alter beliefs about the dangers of continued smoking. Future research should explore the role of provider and social network actions in producing health-related beliefs. It would also be worthwhile to examine whether there are differences between the two groups of survivors in other smoking-related beliefs (e.g., attitudes about quitting smoking) to identify additional potential targets for cessation interventions.

Differences in beliefs may not account for all of the observed differences in successful cessation by cancer type. Survivors of tobacco-related cancers might be using more efficacious cessation strategies (e.g., combined behavioral counseling and pharmacological treatment) than survivors of non-tobacco-related cancer based on recommendations from their clinicians. More research is warranted to explore other potential influences of cessation such as type of cessation strategies used between the two groups of survivors.

This study exhibits several strengths. Data come from a large national U.S. survey that were weighted to adjust for the complex sampling design. The samples of survivors in this study include a wide range of cancer types, which might be more representative of the cancer survivor population than studies of survivors of fewer cancer types. Last, this data included information on when survivors were diagnosed, which allowed for us to examine how relationships between cancer diagnosis and perceived severity of smoking varied over time.

There are two main limitations of the current study. First, type of cancer diagnosis was self-reported, which might not be as accurate as a cancer diagnosis that is confirmed by medical records. Another study, however, used medical records to confirm cancer diagnosis and found a strong correlation—more than 95%— between self-reported diagnosis and medical record-confirmed diagnosis.[49] Second, there were only 80 survivors diagnosed within two years in this sample. Larger studies with more variability in length of time since diagnosis are needed to

ascertain if there are greater differences in perceived risks of smoking between survivors of tobacco and non-tobacco-related cancers in the time shortly after cancer treatment compared to several years after diagnosis.

Conclusions and Implications

In this study, we found differences in perceived severity of health problems from smoking between survivors of tobacco-related and non-tobacco-related cancers that persist years after diagnosis. These findings could potentially in part explain differences in quit rates between the two groups. Longitudinal data are needed to assess whether the perceived severity of health problems from smoking mediates the relationship between diagnosis of tobacco-related cancer and quitting. Additionally, randomized control trials of smoking cessation interventions are needed to test if changing beliefs about the harms of smoking—particularly among survivors of non-tobacco-related cancers—in turn produces higher quit rates. This research underscores the importance of integrating smoking cessation programs into oncology care throughout the survivorship continuum—from diagnosis to long-term follow-up care—and for all smokers, regardless of cancer type. We recommend that clinicians continually assess and discuss beliefs about the harms of continued smoking in survivors of all cancer types and refer patients to evidence-based smoking cessation resources. This approach could particularly benefit survivors of non-tobacco-related cancers—who might not believe smoking is as harmful to their health as other survivors— by underscoring the risks of continued smoking after diagnosis throughout ongoing care.

Table 4.1: Characteristics of the PATH Sample
(*n* = 409 cancer survivors who smoke)

	Total		Tobacco-Related Cancer		Non-Tobacco-Related Cancer	
Characteristic	*n*	%/Mean/SE	*n*	%/Mean/SE	*n*	%/Mean/SE
Cancer Type						
Tobacco-related	174	41.9	---	---	---	---
Non-tobacco-related	235	58.1	---	---	---	---
Gender						
Female	278	64.3	118	63.7	160	64.8
Male	131	35.7	56	36.3	75	35.2
Race						
Non-Hispanic White	327	82.5	140	83.3	187	81.8
Non-Hispanic Black	34	8.3	9	5.2	25	10.5
Hispanic	25	5.5	12	7.2	13	4.2
Other	23	3.8	13	4.2	10	3.4
Completed Education						
Less than HS	128	30.6	61	37.7	67	25.5*
HS graduate	84	24.2	27	17.9	57	28.8
Some college	153	35.2	74	38.6	79	32.7
College degree or more	44	10.0	12	5.8	32	13.0
Time since diagnosis						
≤ 2 years	80	19.5	35	19.8	45	19.2
> 2 years	329	80.5	139	80.2	190	80.8
Age	409	54.0 (0.7)	174	53.0 (1.5)	235	54.8 (0.9)

Percentages, Notes: Means, and standard deviations are weighted.
* Indicates $p < .001$ in chi-square or bivariate regression analyses.

Table 4.2: Linear Regression Analyses
(n = 409 cancer survivors who currently smoke)

	n	Model 1 β (95% CI)	Model 2 β (95% CI)
Diagnosis of tobacco-related cancer			
Non-tobacco-related (ref)	235	—	—
Tobacco-related	174	.25 (.01-.49)*	.23 (-.06-.52)
Race			
Other (ref)	82	—	—
Non-Hispanic White	327	.20 (-.07-.47)	.20 (-.07-.47)
Education			
Less than HS (ref)	128	—	—
HS graduate	281	-.13 (-.35-.09)	-.13 (-.36-.09)
Sex			
Female (ref)	278	—	—
Male	131	-.01 (-.23-.20)	-.01 (-.23-.20)
Age	409	.01 (.01-.02)*	.01 (.01-.02)*
Time since diagnosis			
> 2 years (ref)	329	—	—
≤ 2 years	80	.09 (-.20-0.38)	.05 (-.37-.47)
Diagnosis of tobacco-related cancer (no or yes) × **Time since diagnosis** (> or ≤ 2 years)	409		.09 (-.49-.68)

Notes: * $p < 0.05$
Model 1: Effect of diagnosis of tobacco-related cancer on perceived severity of health problems from smoking, controlling for age, race, sex, education, and time since diagnosis.
Model 2: Effect of diagnosis of tobacco-related cancer on perceived severity of health problems from smoking, controlling for age, race, sex, and education, time since diagnosis, and the interaction term (Diagnosis of tobacco-related cancer × Time since diagnosis).

CHAPTER 5: MANUSCRIPT 3-
DUAL CIGARETTE AND E-CIGARETTE USE IN CANCER SURVIVORS: AN ANALYSIS USING THE POPULATION ASSESSMENT OF TOBACCO HEALTH (PATH) DATA

Introduction. Cancer survivors who smoke cigarettes face multiple health risks from continued smoking and may be particularly motivated to quit. Some smokers use e-cigarettes as a strategy to reduce or quit combustible cigarette use, but research on whether cancer survivors do the same is limited. Research is needed to understand whether cancer survivors use e-cigarettes at higher rates than smokers never diagnosed with cancer, to inform provider-patient discussions about e-cigarettes. **Methods.** Using data from current cigarette smokers in the Population Assessment of Tobacco Health (PATH) study, we examined differences in e-cigarette use and reasons for use among cigarette smokers between cancer survivors (n = 433) and those without a prior cancer diagnosis (n = 10,872). **Results**. Among smokers, nearly 6 in 10 of both cancer survivors and those without a cancer diagnosis have ever used e-cigarettes, and nearly one quarter of both groups currently use e-cigarettes. Results suggest that cancer survivors might be more likely to be ever (OR = 1.28; p=.05) or current (OR = 1.25; p=.06) e-cigarette users compared to those never diagnosed, although these results were marginally significant. The majority of both groups (>71%) reported using e-cigarettes for perceived health-related reasons—including smoking reduction. **Conclusions**. Our study found that among smokers, cancer survivors are using e-cigarettes at similar rates as never-diagnosed smokers and both groups use e-cigarettes largely for perceived health-related reasons. Clinicians may need to

routinely ask their patients who smoke about e-cigarette use and address the limited research on the efficacy of e-cigarettes as a cessation aid as compared to other evidence-based options.

Introduction

The smoking prevalence among cancer survivors ranges widely by cancer type from 7% to 51%.[1,7-10] Smoking rates are especially high in survivors of tobacco-related cancers (e.g., cervical,[1,11-13] bladder,[13] and lung cancer[13]). Researchers estimate that 14% to 64% of cancer survivors who smoked prior to their cancer diagnosis continue to smoke after their diagnosis.[7,10,47,84] Quitting smoking is beneficial for the health of any smoker, but cancer survivors have an even more urgent need to quit because continued smoking after a cancer diagnosis is associated with lower survival,[2,4] higher rates of recurrent disease,[5] more primary tumors,[19-23] decreased efficacy of cancer treatment,[3] and increased treatment-related complications and symptom burden.[6,24,25] Cancer survivors who smoke, as compared to smokers without cancer, are particularly motivated to quit smoking.[39]

Smokers in the general population often perceive and use e-cigarettes (also known as electronic cigarettes or electronic nicotine delivery systems—ENDS) as a strategy to reduce or eliminate combustible cigarette use.[52-54] Research on whether cancer survivors do the same is limited. One study found that 34.3% of cancer survivors who were current conventional cigarette smokers had ever used e-cigarettes, but this study did not compare e-cigarette use rates among current smokers to a population never diagnosed with cancer.[113] Kruse and colleagues analyzed e-cigarette use among adults with and without comorbidities in a large national sample in 2014 and 2015 and found that among current smokers, ever and current e-cigarette use were not different between cancer survivors and the population without any medical comorbidities.[62] This study, however, did not examine differences in use by type of cancer, or account for

demographic characteristics like age.[62] The majority (87%) of cancer survivors in the U.S. are diagnosed at or over age 50,[63] whereas younger age is associated with higher e-cigarette ever use.[64,65] Thus, it might be important to account for differences in age to determine whether survivors are using e-cigarettes at rates beyond what we would expect for their age group.

Few studies have examined e-cigarette use by cancer type. A cross-sectional survey of head and neck cancer patients who were current or former smokers found that 21.7% of patients reported using e-cigarettes as a method to quit smoking.[114] A longitudinal study of currently smoking cancer patients found that a high percentage of thoracic and head and neck cancer patients were e-cigarette users (36.2% compared to 26.5% of survivors of all cancer types), which suggests that e-cigarette use might vary by cancer type.[115] Survivors of tobacco-related cancers might be more motivated to quit smoking combustible cigarettes because of the well-known association between smoking and tobacco-related cancers (e.g., lung cancer). If e-cigarette use rates are relatively high for cancer survivors, and particularly for survivors of specific tobacco-related cancers, then clinicians who treat cancer survivors may need to discuss the current evidence about the cessation efficacy and harms of e-cigarettes with their patients who are trying to quit or reduce smoking.

Although smokers of combustible cigarettes who also use e-cigarettes (i.e., "dual users") often perceive that e-cigarettes help people quit and report using e-cigarettes to attempt to quit or reduce smoking cigarettes,[56,116] the evidence in support of e-cigarettes as a successful smoking cessation strategy is modest and controversial. Two meta-analyses that pooled the results of cohort, cross-sectional, and randomized control trials reported that e-cigarette use was associated with significantly *lower* odds of quitting smoking combustible cigarettes.[55,56] Studies included in these meta-analyses, however, have been criticized as being limited by selection bias, low

reliability, and confounders.[117] In contrast, two other meta-analyses—including a Cochrane review, which included only randomized control studies, found that e-cigarette users were *more* likely to quit conventional cigarettes if their e-cigarettes contained nicotine versus if they did not contain nicotine.[57,58] There is one published randomized control trial that compared e-cigarettes to another other smoking cessation method—nicotine replacement therapy (NRT), but there were no significant differences in quit rates between the intervention arms[59] and this trial had significant methodological limitations.[56] In a systematic review of the literature on e-cigarettes and smoking cessation, Malas and colleagues point out that it is unclear whether e-cigarettes only help certain types of smokers reduce or quit cigarette use, and if their efficacy changes with the use of other cessation aids such as counseling or NRT.[117] Thus, as the literature currently stands, the evidence is inconclusive that e-cigarettes help smokers—including both cancer survivors and those never diagnosed—quit combustible cigarettes. The authors of three systematic reviews of smoking cessation interventions for cancer survivors recommend that cancer survivors receive the gold standard for smoking cessation treatment in the general population: a combination of FDA-approved medication—mainly nicotine replacement therapy and varenicline— and behavioral therapies such as counseling and reading materials.[37-39]

In addition to the limited research on the efficacy of e-cigarettes as a smoking cessation tool, there are known short-term harms of e-cigarette use, although more research is needed to document long-term health consequences of using e-cigarettes specifically in cancer survivors. Meernik and Goldstein argue that clinicians should not recommend e-cigarettes to their patients who are trying to quit smoking because of safety concerns (e.g., burns and other injuries) and clinicians' ethical framework to do no harm.[60] The potential interactions of e-cigarettes and cancer therapies are also unknown.[61] E-cigarettes are thought to be less toxic than conventional

cigarettes, but they still contain hazardous chemicals that could increase a smoker's risk for disease, and the long-term health risk of e-cigarettes is currently unknown,[118] particularly among cancer survivors who are already at higher risk for developing cancer than the general population.[119] It is currently unclear if the benefits of e-cigarettes as a smoking cessation tool outweigh the potential harms in cancer survivors.

There are several gaps in the literature on patterns of e-cigarette use and reasons for use in cancer survivors who smoke combustible cigarettes as they compare to smokers never diagnosed with cancer. It is possible that cancer survivors, who may be more motivated to quit smoking than smokers without a prior cancer diagnosis,[39] are more likely to report using e-cigarettes for health-related reasons (e.g., to cut back on smoking). In the current study, we used national data to examine two research questions: 1) Does the prevalence of e-cigarette use among current combustible cigarette smokers vary by cancer survivorship status and cancer type?; and 2) Do reasons for e-cigarette use among smokers vary by cancer survivorship status?

Methods

Data Source and Sample

We used data from Wave 1 of the Population Assessment of Tobacco Health (PATH) study, funded by the National Institutes of Health, through the National Institute on Drug Abuse, and the Food and Drug Administration (FDA).[112] The PATH study is a national longitudinal survey on tobacco use behavior that sampled tobacco users and non-users in the U.S (N = 32,320 adults). The PATH study over-sampled tobacco users, young adults aged 18-24, and African Americans. The PATH methodology is described elsewhere.[112] The analytic sample used to assess differences in e-cigarette use by cancer survivorship status consisted of all adult (age 18 and above) current conventional cigarette smokers who reported their cancer survivorship status

(n=11,305). The analytic sample used to compare e-cigarette use by cancer type consisted of 433 cancer survivors who currently smoked conventional cigarettes. The analytic sample used to assess differences in reasons for e-cigarette use by cancer survivorship status consisted of all current e-cigarette users who reported reasons for use (n = 2,510). Data were collected between 2013-2014 by audio computer-assisted self-interviewing (ACASI) and computer-assisted personal interviewing (CAPI) questionnaires. The Institutional Review Board at the University of North Carolina at Chapel Hill exempted the secondary analyses of PATH data as not human subject research.

Measures

Cancer Survivorship Status. A dichotomous cancer survivorship status variable was defined based on participant response to the question "Have you ever been told by a doctor or other health professional that you had cancer?" with "yes" responses categorized as cancer survivors.

Diagnosis of Tobacco-Related Cancer. To assess variation in e-cigarette use by cancer type, we derived a dichotomous indicator of whether a cancer survivor was diagnosed with a cancer that was tobacco-related or not tobacco-related from the PATH questions about cancer diagnosis. Participants who indicated having a cancer diagnosis were asked, "What kind of cancer?" We classified cancers that are tobacco-related using the 2009 International Agency for Research on Cancer (IARC) guidelines on cancers related to tobacco use,[103] as has been done in previous studies.[17,47,49] Tobacco-related cancers are cancers of the bladder, cervix, colon, esophagus, kidney, larynx/windpipe, liver, lung, mouth/tongue/lip, pancreas, stomach, throat, and uterus; all other types were considered non-tobacco related. Non-melanoma skin cancer and

“other cancer” responses were not included in these analyses because these cancers are not typically included in studies that assess cigarette use in cancer survivors.

Cigarette Use. All participants were asked whether they smoked at least 100 cigarettes in their life. Those who indicated they had were further asked whether they currently smoke cigarettes "every day," "some days," or "not at all." Current smokers were characterized as those who smoked at least 100 cigarettes in their lifetime and currently smoked every day or some days.

E-cigarette Use. We constructed two measures of e-cigarette use: ever use and current use. After a brief introduction to e-cigarettes, PATH participants were asked, “Have you ever used an e-cigarette, such as NJOY, Blu, or Smoking Everywhere, even one or two times?” Participants were categorized as ever users of e-cigarettes or never-users of e-cigarettes. Ever users of e-cigarettes were also asked, “Do you now use e-cigarettes…Every day, Some days, or Not at all.” Those who responded “Every day or some days” were considered current users. Participants were also asked, “How old were you when you first started using an e-cigarette, even one or two times?” and provided their age in years. We created a dichotomous variable to determine whether cancer survivors started using e-cigarettes before they were diagnosed or after diagnosis by subtracting their age at first e-cigarette from their age at diagnosis. Cancer survivors who first used e-cigarettes the year they were diagnosed were coded as having first used e-cigarettes after diagnosis.

Reasons for E-cigarette Use. Participants who reported currently using e-cigarettes were asked a series of yes or no questions about 13 reasons they use e-cigarettes. Four questions were related to health. These health-related reasons include: “they might be less harmful than cigarettes,” “they can help people to quit smoking,” “they might be less harmful to others than

cigarettes," and "they can be a way of cutting down on cigarette smoking." Participants answered nine questions about e-cigarette use that were unrelated to health (e.g., "they came in flavors I liked", "it feels like smoking a regular cigarette," "I could use e-cigarettes at times when or in places where smoking cigarettes wasn't allowed," "People who are important to me use e-cigarettes.") We analyzed each of the 13 reasons separately.

Additional Variables: In some analyses we included as covariates measures of age (in years), race/ethnicity (1=non-Hispanic White or 0=other race/ethnicity), education (0=less than high school education and 1=high school education and above), and gender (0=female or 1=male) because these variables are related to e-cigarette use in the general population[64,65] and in cancer survivors.[113]

Analytic Strategy

We calculated descriptive statistics for all outcome variables. We used SAS version 9.3 to conduct all analyses, using the PATH survey weights to compensate for variable probabilities of selection, differential nonresponse rates, and possible deficiencies in the sampling frame (e.g., the under coverage of certain population groups). We examined the extent and pattern of missing data for all covariate variable measures. No variables were missing at a rate higher than 5%; cases with data missing on predictor or control variables were dropped in logistic regression tests.

Prevalence of e-cigarette use: We conducted logistic regression analyses to examine differences in e-cigarette ever use and current use between cancer survivors and those without a cancer history, controlling for age, income, race, and education; we had complete information for n = 10,548 participants. Given the smaller sample of e-cigarette users with a cancer diagnosis,

we relied on chi-square analyses to examine differences in e-cigarette use between survivors of tobacco-related and non-tobacco-related cancers.

Reasons for e-cigarette use: We conducted chi-square analyses to examine whether there were significant differences in reasons for e-cigarette use as a function of cancer survivorship status.

Results

Table 1 describes characteristics of the 11,305 PATH participants who were current combustible cigarette smokers, stratified by cancer status. Cancer survivors, as compared to those without a prior diagnosis of cancer, were significantly more likely to be female (64.5% vs. 43.7%), non-Hispanic White (82.4% vs. 69.1%, respectively), have a less than high school education (31.5% vs. 26.4%), and were older (mean age 54.2 years vs. 41.1 years).

Ever E-cigarette Use.

Among current smokers, 59.4% of cancer survivors reported ever using an e-cigarette compared to 63.2% of those never diagnosed with cancer (Table 1). In logistic regression analyses controlling for race, education, sex, and age (Table 2), cancer survivors had 1.28 times the odds of ever using e-cigarettes compared to those without a history of cancer (OR = 1.28; 95% CI: 1.01-1.63; p=.0457). In this sample, 90% of cancer survivors who ever used e-cigarettes first tried them during the year of diagnosis or sometime after diagnosis.

There were no significant differences in ever e-cigarette use between survivors of tobacco-related cancers and those diagnosed with non-tobacco-related cancers (62.5% versus 57.4%, respectively; χ^2= 0.93; p=.33; results not reported in Table 2).

Current E-cigarette Use.

Among cancer survivors who were current smokers, 23.1% reported currently using e-cigarettes every day or some days compared to 22.3% of those who have never been diagnosed with cancer (Table 1). In adjusted logistic regression analyses (Table 2), cancer survivors had 1.25 times the odds of currently using e-cigarettes compared to those without a history of cancer, but this association was marginal (OR = 1.25; 95% CI: 0.99-1.58; p=.06).

Rates of current e-cigarette use between those diagnosed with tobacco-related cancers and those diagnosed with non-tobacco-related cancers (23.8% versus 22.6%) did not differ significantly (χ^2= 0.08; p=.78; results not reported in Table 2).

Reasons for E-cigarette Use.

Table 3 displays the reasons why current e-cigarette users who smoke reported using e-cigarettes in cancer survivors and in the general population without a cancer history. The majority of both cancer survivors (ranging from 75%-88%) and those without a prior cancer diagnosis (ranging from 72%-85%) reported using e-cigarettes for health-related reasons (e.g., "they might be less harmful to people around me than cigarettes.") Similarly, the majority of both cancer survivors and those never diagnosed with cancer endorsed using e-cigarettes because they could use them at times when or in places where smoking cigarettes was not allowed (>83%) and because e-cigarettes do not smell (>76%). Most cancer survivors and those without a history of cancer who currently use e-cigarettes did not report using e-cigarettes because people in the media or other public figures use e-cigarettes, because people who are important to them use e-cigarettes, or because the advertising of e-cigarettes appeals to them. In chi-square analyses for each reason for using e-cigarettes, contrary to our expectation, cancer survivors were not more likely to report using e-cigarettes for health-related reasons than smokers without a prior

cancer diagnosis. We found significantly more people never diagnosed with cancer selected "people who are important to me use e-cigarettes" as a reason for using e-cigarettes compared to cancer survivors (χ^2= 5.16; p=.02), although this significant *p*-value could have been detected by chance.

Discussion

This national study found that nearly 6 in 10 cancer survivors who smoke have also used e-cigarettes, and nearly one quarter of survivors are currently doing so, regardless of cancer type. These rates were similar to those without a prior cancer diagnosis. In this sample, 90% of cancer survivors who ever used e-cigarettes first tried them during the year of diagnosis or after they were diagnosed and more than 75% of the cancer survivors who reported dual use of cigarettes and e-cigarettes cited health-related reasons for their e-cigarette use, including smoking reduction or cessation. This suggests that a substantial number of smokers may try e-cigarettes as a cessation strategy following a cancer diagnosis.

Similar to the study by Kruse et al.,[62] we observed no differences in e-cigarette use prevalence of cancer survivors when compared to non-cancer survivors, although once we adjusted for age, race/ethnicity, education, and gender, cancer survivors were more likely to ever use e-cigarettes and marginally more likely to currently use e-cigarettes. Larger samples are needed to confirm whether there might be a difference in e-cigarette use between cancer survivors and a population without a prior cancer diagnosis, adjusting for age, education, race/ethnicity, and gender.

We also found that cancer survivors report currently using e-cigarettes for the same reasons as the general population. The majority of dual current e-cigarette and combustible cigarette users indicated they use e-cigarettes because they might be less harmful to themselves

or others, could be used at times when smoking cigarettes was not allowed, they do not smell, or could help people quit smoking. It does not appear that experiencing a cancer diagnosis motivates people to use e-cigarettes for health-related reasons more so than those never diagnosed with cancer because the majority (more than 72%) of both groups report that they use e-cigarettes for health-related reasons, although larger studies are needed to better understand this relationship.

Clinicians who treat cancer patients who smoke, regardless of cancer type, may therefore want to discuss the current evidence about the cessation efficacy and harms of e-cigarettes, along with evidence-based cessation methods such as pharmacotherapy (e.g., NRT, varenicline, bupropion) and behavioral counseling (e.g., skills training, stress management),[10,39] when asking their patients about their cessation efforts. By discussing that the efficacy and harms of e-cigarettes use in smoking cessation are currently unknown, clinicians may help change patient perceptions that e-cigarettes will help them quit or reduce smoking, and encourage techniques for which the evidence base is stronger. It may be important for clinicians to have these discussions with their patients who smoke throughout primary care, even before patients are diagnosed with cancer because both cancer survivors and those without a cancer history cited health-related reasons for using e-cigarettes. Thus, it might be worthwhile for clinicians to follow the emerging literature about the cessation efficacy and harms of e-cigarettes to best advise their patients about the most effective cessation options.

There are several strengths to this study. Data come from a large national U.S. survey that were weighted to adjust for the complex sampling design. These data include information on cancer diagnosis, which allows for comparison of e-cigarette use and reasons for use between survivors and those never diagnosed with cancer. The data also include an assessment of current

e-cigarette use, which might better describe the extent that cancer survivors who smoke are using e-cigarettes as a smoking cessation tool than if the data only contained information about ever use, where it would have been difficult to differentiate between those who only used e-cigarettes experimentally from those who use more frequently.

There are several limitations of this study that are important to keep in mind. First, the number of cancer survivors who reported currently using e-cigarettes was small (n = 99) and results should be interpreted with caution because they might not generalize to all cancer survivors who are dual users of e-cigarettes and cigarettes. This sample size precluded us from controlling for demographic characteristics when analyzing differences in reasons for using e-cigarettes. The samples of current e-cigarette users who were cancer survivors and those never diagnosed, however, were not significantly different in age or education—two factors related to e-cigarette use.[64,65] The limited sample size might also contribute to non-significant differences in e-cigarette use between survivors of tobacco-related and non-tobacco-related cancers. Larger studies of e-cigarette use and reasons for use in cancer survivors are needed, with a focus on differences between survivors of various cancer types. Second, cancer diagnosis in this study was self-reported, which might not be as accurate as a diagnosis confirmed by medical records. Another study, however, used medical records to confirm cancer diagnosis and found a strong correlation—more than 95%— between self-reported diagnosis and medical record-confirmed diagnosis.[49]

Conclusions and Implications

Our results indicate that cancer survivors using e-cigarettes at similar rates as those without a cancer history. Many current cigarette smokers—regardless of whether they have been diagnosed with cancer or not—are using e-cigarettes because they perceive that e-cigarettes will

help them quit smoking cigarettes or reduce their cigarette consumption. Oncology clinicians should recognize that up to a quarter of their patients who smoke might be currently using e-cigarettes as a perceived harm reduction tool. It would be worthwhile for clinicians who treat cancer survivors to stay abreast of research related to the efficacy and harms of e-cigarettes as a smoking cessation tool and to discuss any misconceptions about e-cigarettes with their patients who are trying to quit smoking.

Table 5.1: Characteristics of PATH participants

	Cancer[a] *n* = 433		**No Cancer** *n* = 10,872		**Total** *n* = 11,305		
Characteristic	*n*	%/Mean (SE)	*n*	%/Mean (SE)	*n*	%/Mean (SE)	***p*-value**[b]
Sex							
Female	296	64.5	5,064	43.7	5,360	44.6	<.0001
Male	137	35.5	5,804	56.3	5,941	55.4	
Race							
Non-Hispanic White	336	82.4	7,059	69.1	7,395	69.7	<.0001
Non-Hispanic Black	35	8.4	1,421	13.2	1,456	13.0	
Hispanic	26	5.4	1,420	11.6	1,446	11.3	
Other	24	3.7	804	6.1	828	6.0	
Completed Education							
Less than HS	138	31.5	3,023	26.4	3,161	26.6	.02
HS graduate	87	23.8	2,768	28.1	2,855	28.0	
Some college	160	34.4	3,873	33.6	4,033	33.6	
College degree or more	45	9.8	1,145	11.2	1,190	10.3	
Age	433	54.2 (0.7)	10,871	41.1 (0.2)	11,304	41.7 (0.2)	.01
Ever E-cigarette User[c]	250	59.4	6,791	63.2	7,041	63.1	.16
Tobacco-related	108	62.5	--	--	--	--	
Non-tobacco-related	142	57.4	--	--	--	--	
Current E-cigarette User	99	23.1	2,411	22.3	2,510	22.3	.70
Tobacco-related	44	23.8	--	--	--	--	
Non-tobacco-related	55	22.6	--	--	--	--	

Notes: Means and percentages are weighted.
[a]58.2% of cancer survivors were diagnosed with non-tobacco-related cancers.
[b]*p* values from Rao-Scott chi-square test or bivariate linear regression analyses.
[a]90% of cancer survivors who ever used e-cigarettes first tried them during the year of diagnosis or after they were diagnosed.

Table 5.2: Logistic Regression Analyses
n = 10,548

		Ever E-cigarette Use		Current E-cigarette Use	
	n	OR (95% CI)	***p*-value**	OR (95% CI)	***p*-value**
Cancer Diagnosis					
No history of Cancer (ref)	10,154	—		—	
Cancer Survivor	394	1.28 (1.01-1.63)	.05	1.25 (0.99-1.58)	.06
Race					
Other (ref)	3,453	—		—	
Non-Hispanic White	7,095	1.62 (1.47-1.77)	<.0001	1.33 (1.17-1.50)	<.0001
Education					
Less than HS (ref)	2,894	—		—	
HS graduate	7,654	1.09 (0.98-1.22)	0.11	1.20 (1.06-1.35)	<.001
Sex					
Female (ref)	5,016	—		—	
Male	5,532	0.81 (0.75-0.88)	<.0001	0.91 (0.83-1.00)	.05
Age (Measured continuously)	10,548	0.96 (0.96-0.97)	<.0001	0.98 (0.98-0.99)	<.0001

Table 5.3: Reasons for current e-cigarette use
n = 2,510

	Cancer *n* = 99		No Cancer *n* = 2,411		Total *n* = 2,510		
Reason for E-cigarette Use	*n*	%	*n*	%	*n*	%	***p*-value[a]**
Health-Related Reasons							
They might be less harmful to me than cigarettes	77	78.4	1,935	80.5	2,012	80.4	.64
They might be less harmful to people around me than cigarettes	86	87.5	2,043	85.1	2,129	85.2	.52
Using them help people to quit smoking	69	74.5	1,727	71.9	1,796	72.0	.52
Used them as a way of cutting down on cigarette smoking	79	80.1	1,693	71.8	1,772	72.2	.11
Non-Health-Related Reasons							
People in the media or other public figures use e-cigarettes	21	19.0	429	18.0	450	18.0	.83
Could use e-cigarettes at times when or in places where smoking cigarettes wasn't allowed	90	88.9	2,017	83.5	2,107	83.8	.33
Came in flavors I liked	64	65.8	1,586	63.8	1,650	63.9	.72
E-cigarettes don't smell	78	81.2	1,827	76.1	1,905	76.3	.33
Feels like smoking a regular cigarette	45	46.0	1,091	47.3	1,136	47.2	.79
More acceptable to non-tobacco users	66	68.1	1,698	70.7	1,764	70.6	.58
People who are important to me use e-cigarettes	13	10.8	451	18.9	464	18.5	.02
I like socializing while using an e-cigarettes	41	40.8	898	37.2	939	37.4	.50
The advertising for e-cigarettes appeals to me	14	12.6	469	19.4	483	19.1	.07

Notes: Percentages are weighted.
[a]*p* values from Rao-Scott chi-square test

CHAPTER 6: SUMMARY AND DISCUSSION

6.1 Summary of Research Findings

The purpose of this dissertation was to better understand smoking-related factors uniquely influenced by receiving a cancer diagnosis that could be targeted in smoking cessation interventions to improve quit rates and ultimately reduce morbidity and mortality outcomes among cancer survivors. This dissertation examined psychosocial predictors of both smoking cessation and the length of time it took survivors to quit, diagnosis of a tobacco-related cancer as a correlate of perceived severity of health problems from smoking, and whether cancer survivors who smoke are using e-cigarettes—a perceived harm reduction strategy—to help them reduce or quit smoking.

Manuscript 1: Psychosocial Factors and Quitting Smoking in Long-Term Cancer Survivors

In Manuscript 1, I hypothesized that survivors with higher psychological distress, lower HRQOL, and lower perceived social support at one year after diagnosis would be less likely to quit smoking within 10 years of diagnosis and would take longer to quit compared to those with lower psychological distress, higher HRQOL, and higher perceived social support. Of the four psychosocial variables that I examined in this sample, only physical HRQOL was significantly associated with smoking cessation and when cessation occurred. Cancer survivors with low physical HRQOL were both significantly less likely to quit smoking when controlling for cancer type and number of comorbid conditions and took several more years to quit than survivors with high physical HRQOL. The first noticeable increase in the probability of quitting occurred at 2

years after diagnosis in survivors with high physical HRQOL compared to year 6 in survivors with low physical HRQOL. Survivors of tobacco-related cancer with high physical HRQOL were the most likely group to quit smoking, while survivors of tobacco-related cancer with low physical HRQOL were the least likely group to quit.

Manuscript 2: Diagnosis of Tobacco-Related Cancer and Perceived Severity of Health Problems from Smoking

In Manuscript 2, I hypothesized that survivors of tobacco-related cancers would report greater perceived severity of health problems caused by smoking than survivors of non-tobacco-related cancers and that the difference in perceived severity between the two groups would be largest in survivors who had been diagnosed within two years. In partial support of my hypotheses, I found that survivors of tobacco-related cancer reported higher perceived severity of health problems from smoking than survivors of non-tobacco-related cancer, but contrary to my expectation, this relationship was the same for survivors diagnosed within two years and for long-term survivors.

Manuscript 3: Dual cigarette and e-cigarette use in cancer survivors

In Manuscript 3, I examined whether the prevalence of e-cigarette use among current combustible cigarette smokers varied by cancer survivorship status and cancer type and whether reasons for e-cigarette use varied by cancer survivorship status. I found that nearly 6 in 10 cancer survivors who smoke have also used e-cigarettes, and nearly one quarter of survivors are currently doing so, regardless of cancer type. Prevalence rates of ever e-cigarette use and current e-cigarette use were similar in cancer survivors and those without a cancer history. Results suggest that cancer survivors might be even more likely to ever or currently use e-cigarettes compared to those without a prior cancer diagnosis, although associations in this sample were marginally significant. In this sample, cancer survivors reported currently using e-cigarettes for

the same reasons as the general population; the majority of both groups (>71%) reported using e-cigarettes for perceived health-related reasons—including smoking reduction.

6.2 Strengths and Limitations

This dissertation possesses several strengths. First, both datasets used in these analyses (SCS-I and PATH) were large national datasets that included rich information on cancer survivors, including the type of cancers with which survivors were diagnosed and when they were diagnosed. These data are helpful for identifying populations that might need more intensive smoking cessation resources and ideal times to intervene. For example, Manuscript 1 identified that survivors with low physical HRQOL—and particularly those diagnosed with tobacco-related cancers—were less likely to quit smoking and took longer to quit smoking among those who did quit than others, and thus might need to be targeted with intensive cessation resources that span several years after diagnosis to address their unique barriers to quitting. Manuscript 2 found that survivors of non-tobacco-related cancer—both those recently diagnosed and longer-term survivors— had lower perceived severity of health problems from smoking, which indicates that clinicians should work to increase the perceived harm of smoking in those survivors throughout the cancer continuum.

Second, the longitudinal nature of the SCS-I dataset used in Manuscript 1 made it possible to use time-to-event analysis to identify not just who was less likely to quit smoking but also how much longer it took certain groups to quit, which has implications for which groups to continue to provide intensive cessation resources over time.

Finally, the PATH data included measures of both ever and current e-cigarette use, which provided information about both experimental e-cigarette users (e.g., those who used e-cigarettes one or two times) and those who use more frequently. These two measures of e-cigarette use

provide a fuller picture of the extent that cancer survivors who smoke are using e-cigarettes as a smoking cessation tool than if only one measure of e-cigarette use were assessed.

Some limitations of this dissertation relate to the measures used in each dataset. In Manuscript 1, the variable time since quitting was imprecisely measured because age at quitting was measured in discrete years, which might not reflect an accurate time of when survivors quit smoking. The yearly hazard ratio of quitting smoking, however, has been used in another time-to-event analysis study[106] and I incorporated the discrete nature of the data into the analyses. More precise measures of the length of time until quitting in days or months, rather than in years, may help us better understand the best windows of opportunity for intervention. Second, in SCS-I, smoking status was assessed retrospectively at a single time point. It would be informative for future studies to conduct these analyses in data that contain multiple assessments of both psychosocial factors and smoking status over time to improve our understanding of the directionality of this association and to ensure more precise measurement of the timing of cessation. Third, in the PATH data, cancer type was self-reported, unlike in SCS-I, where cancer type was confirmed by medical records. Self-reported cancer diagnosis might not be as accurate as a confirmed cancer diagnosis, although Westmaas et al. found a strong correlation (>95%) between self-reported diagnosis and medical record-confirmed diagnosis in the SCS-I data.[49]

This dissertation also includes limitations in generalizability of findings. First, the analysis in Manuscript 1 relies on data from longtime cancer survivors and the generalizability of any findings from this work has to be understood as applicable only to individuals who do survive 7-10 years post diagnosis. In the SCS-I sample, participants in Wave 1 were more likely to remain in Wave 3 if they were diagnosed with non-tobacco-related cancer and reported lower comorbid conditions at Wave 1, lower psychological distress, higher mental and physical

HRQOL, and higher perceived social support. The smoking rate was low in the SCS-I Wave 3 sample (7.8%); if the people lost to follow-up were also particularly unlikely to quit smoking and were perhaps heavier smokers and had worse psychosocial outcomes, had I included them in the analytic sample, results might have been different. Second, some analyses in Manuscripts 2 and 3 had limited sample sizes, so null results might reflect limited power to detect smaller effects. In Manuscript 2, there were only 80 survivors diagnosed within two years, thus larger studies with more variability in length of time since diagnosis are needed to ascertain if there are greater differences in perceived severity of smoking between survivors of tobacco and non-tobacco-related cancers in the time shortly after cancer treatment compared to several years after diagnosis. In Manuscript 3, only 99 cancer survivors reported currently using e-cigarettes so generalizing about the reported prevalence of different reasons for use should be done with caution. This sample size also precluded us from controlling for demographic characteristics when analyzing differences in reasons for using e-cigarettes. The samples of current e-cigarette users who were cancer survivors and those never diagnosed, however, were not significantly different in age or education—two factors related to e-cigarette use.[64,65] It is possible that we did not find significant differences in e-cigarette use between survivors of tobacco-related and non-tobacco-related cancers because our sample size was not large enough to detect a statistical difference. Larger studies of e-cigarette use and reasons for use in cancer survivors are needed, with a focus on differences between survivors of various cancer types.

Reasons for using two different datasets. This dissertation relied on data from multiple datasets because no single dataset contained information necessary to explore all of my research questions. I decided to use the SCS-I dataset in Manuscript 1 of this dissertation because it had multiple psychosocial predictors at Wave 1 that were theoretically relevant to smoking cessation

in cancer survivors and it was longitudinal, which allowed me to use time-to-event analysis to answer my questions. SCS-I included one item on perceived severity of health problems from smoking, but I chose to use the PATH dataset in Manuscript 2 to examine differences in perceived severity between survivors of tobacco-related and non-tobacco-related cancers because 1) PATH also contained data from recently diagnosed and long-term survivors, which allowed me to test for an interaction with time since diagnosis, 2) PATH had two items that measured perceived severity of smoking, which was more informative than one item, and 3) PATH had a larger sample size and included more cancer types than SCS-I. I chose to use PATH to answer the research questions in Manuscript 3 because this was the only dataset that included information on e-cigarette use and reasons for use in cancer survivors.

6.3 Implications for Research and Practice

Implications for Research

The results from all three studies highlight important additional avenues of research that could enhance our understanding of smoking cessation in cancer survivors. First, longitudinal studies that track beliefs, behaviors, and smoking statuses of cancer survivors progressively over time would allow for more precise measurement of many of the constructs employed in this dissertation, and testing of some of the mediation pathways inherent in the theoretical models driving the studies here. For example, annual measures of smoking-related beliefs, quit intention, and smoking status over time would extend the research in the second manuscript to assess whether beliefs about smoking mediate the relationship between diagnosis of tobacco-related cancer and both quit intentions and successful quitting. Additionally, charting dual combustible and electronic cigarette use in survivors over time could improve our understanding of how e-

cigarettes are used as cessation strategies, and whether they are effective in survivors who may be especially motivated to quit.

Second, datasets that include other psychosocial constructs, such as attitudes about quitting smoking (i.e., barriers and benefits to quitting and benefits to smoking) and provider and social network actions related to cessation (e.g., whether there are other smokers in the house, whether survivors experienced social pressure to quit from their friends and family, attitudes and beliefs about quitting of the smokers' social network, and whether clinicians advised cancer patients to quit and cessation strategies they recommended), could add to the research on why cancer type is associated with smoking cessation. Additionally, it would be informative to assess psychosocial constructs such as a survivor's fatalistic beliefs—i.e., the belief that one's own actions will not influence health, which can undermine health-protective behaviors in cancer survivors[69]—to explore why survivors with poor physical HRQOL particularly struggle to quit smoking. In the theoretical models for this dissertation, I combined constructs across several theories that I thought were the most pertinent in explaining why a cancer diagnosis might influence smoking behavior, but it is possible that theoretical constructs not included in this dissertation (e.g., self-efficacy for quitting, subjective norms, perceived behavioral control) could also be important links between cancer type, psychosocial variables, and cession. An alternative model building approach would have been to test all of the constructs in each theory separately to identify variables that might be most salient, and then combine those to produce an overall conceptual model. Unfortunately, key measures of all constructs of any theory were not available or reliable in the data, but future work that took this approach could identify additional targets for intervention.

Third, intervention research could examine lingering questions about whether changing the predictors assessed in this dissertation actually produce expected changes in smoking. For example, although the first study identified physical HRQOL as a risk factor for smoking and delayed cessation, it is unclear whether it is a causal factor. Research could test whether strategies to mitigate physical symptoms in those with poor physical HRQOL (e.g., by incorporating acupuncture or occupational therapy to combat persistent fatigue and pain) increase the likelihood of successful smoking cessation. If such strategies prove ineffective, researchers should explore potential correlates of physical HRQOL that might be causally related to smoking. Similarly, randomized control trials of smoking cessation interventions could test whether changing beliefs about the harms of smoking—particularly among survivors of non-tobacco-related cancers—in turn produces higher quit rates.

Finally, qualitative studies could shed additional light on the quantitative findings in this dissertation. In-depth interviews with cancer survivors could further our understanding of: 1) why survivors with low physical HRQOL struggle to quit smoking (e.g., Which specific barriers to quitting do survivors with low physical HRQOL experience?), 2) how messages from providers and family members influence their smoking-related health beliefs, 3) survivors' beliefs about the effectiveness of e-cigarettes as a cessation tool, especially as compared to other cessation strategies, and 4) which cessation strategies survivors tried and which have been the most successful.

Implications for Practice

The findings from all three Manuscripts have implications for clinical practice with cancer survivors who smoke. Having a diagnosis of a non-tobacco related cancer is associated with lower perceived risks from smoking and lower quit rates, so clinicians should identify and

discuss health problems related to smoking with all of their patients who smoke, but particularly with their patients diagnosed with non-tobacco-related cancers.

Asking a few additional questions about smoking may also enhance the ability of clinicians to support cessation. By assessing physical HRQOL and perceived severity of smoking as part of routine care, clinicians can identify patients at particularly high risk to continue smoking and work with them to understand their risks and identify resources for cessation assistance. Survivors with low physical HRQOL may particularly need intensive long-term smoking cessation interventions that include strategies to help them manage their symptoms (e.g., strategies that reduce pain and fatigue).

By asking whether smokers are trying e-cigarettes as a strategy for quitting, providers can also identify patients who may need additional information about the risks and potential benefits of e-cigarette use, and provide them with alternative evidence-based strategies. To counsel about this effectively, it would be worthwhile for clinicians themselves to stay abreast of the still emerging literature about the cessation efficacy and harms of e-cigarettes.

6.4 Conclusions

Quitting smoking is beneficial to the health of any person, but particularly for cancer survivors who are susceptible to even more health issues than the general population if they continue to smoke.[15] Smoking cessation treatment programs in oncology settings are rare[15,36] and the few smoking cessation interventions for cancer survivors that have been implemented have not been effective in influencing smoking cessation rates.[37] Based on the findings from this dissertation, clinicians may want to assess physical HRQOL, perceived severity of smoking, and e-cigarette use as a quitting strategy in their patients who smoke to identify patients at

particularly high risk of continued smoking and potential means for interventions that could address the unique needs of cancer survivors.

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