
Practice Guideline:

Supportive Care

Smoking Cessation in Oncology Care

Effective: November 2015

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Updated:

Preface

At CancerCare Manitoba (CCMB) the Clinical Practice Guidelines Initiative seeks to improve patient outcomes in terms of survival and quality of life through the development, dissemination, implementation and evaluation of guidelines for the management of common clinical scenarios encountered by cancer patients throughout the province.

This practice guideline was created through the efforts of a small interdisciplinary working group from CCMB. Members of the Department of Nursing, the Provincial Pharmacy Program and Psychosocial Oncology have participated in its development.

The working group will review and update this document every two years, unless emerging evidence from scientific research, or practice issues requiring urgent resolution dictate a need for more immediate change in content.

Purpose

This document is intended as a guide to facilitate an evidence-based, shared approach to the clinical support of smoking cessation within oncology care.

For this purpose, it may be used by qualified and licensed healthcare practitioners involved with the care of oncology patients, which may include (but is not limited to): physicians, surgeons, nurses, radiation therapists, pharmacists, psychosocial oncology caregivers, and dieticians at CCMB, and Community Oncology Program sites (Community Cancer Programs Network (CCPN) sites, Uniting Primary Care and Oncology Network (UPCON) sites and WRHA Community Oncology Program sites).

Disclaimer

This guideline document should be viewed as an evidence-based practice tool, and as such, it does not represent an exhaustive text on the subject of smoking cessation in oncology. Clinicians are advised to use it in their practice concomitantly with information from other evidence-based sources.

Use of this guideline in the clinical setting should not preclude use of the practitioner's independent clinical judgment, nor should it replace consultation with the appropriate oncology specialist when indicated (example: medical oncologist, radiation oncologist, family practitioner in oncology (FPO), nurse practitioner/clinical nurse specialist, pharmacist, psychosocial oncology professional and dietician).

It is the responsibility of the practitioner to develop an individualized disease or symptom management plan for each patient under his/her care, and ideally, this should take place within the context of a multidisciplinary team. The needs and preferences of the patient and the family should always be reflected in the plan of care.

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Guideline Recommendations

1. To enhance quality of life, patients with any type of cancer should be encouraged to quit smoking at any point in their journey by their oncologists and by other oncology team members.
2. Clinicians should approach quality of life discussion from the perspective of the patient's context including family members, patient environment, and cultural norms of practices which are important factors to include in smoking cessation strategies.
3. Education regarding smoking cessation coping strategies should be incorporated into the care of cancer patients.
4. Adult smokers should quit smoking after a cancer diagnosis. Evidence suggests that those who quit will have improved prognosis, lower relapse/recurrence rates and fewer second primary tumours.
5. Patients who smoke should be encouraged to stop. Stopping at any point during the cancer treatment journey is found to be beneficial. Smoking cessation can decrease treatment-related toxicity and improve tolerance. It also decreases late effects of surgery/recovery, radiation, chemotherapy and drug treatments.

CancerCare Manitoba

Supportive Care Recommendations

Smoking Cessation in Oncology Care

I. Introduction

The association between cancer and first and second hand smoke was established nearly 50 years ago.¹ To date, tobacco use has been implicated in the following cancers: lung, oral cavity, esophageal, pharynx, pancreas, liver, kidney, ureter, urinary bladder, uterine cervix, endometrial, ovarian, prostate, colorectal, breast and myeloid leukemia.²⁻⁴ Evidence has further shown that 30% of all cancer-related deaths are due to smoking tobacco.^{2,4-6} As a consequence of smoking, ever-smokers (current and former smokers) have a 5.6 times greater risk of developing lung cancer and a 2.5 times greater risk of developing bladder cancer than never smokers – with females at a significantly higher risk of developing bladder cancer than men who smoked comparable quantities of cigarettes.⁷⁻⁹ Disease-specific statistics for head and neck cancer suggest that 85% of the 53,000 cases diagnosed in the United States each year are tobacco-related.¹ Other disease-specific statistics are similar.^{2,5,10,11} In Canada, smoking is related to more than 85% of lung cancer cases.¹² As a result, tobacco use is considered to be the foremost preventable cause of cancer and the world's leading cause of premature death.^{2-4,13} Unsurprisingly, it has been listed as one of the most important public health problems of our time.¹

A report addressing the patterns and trends of tobacco use in Canada suggests that 16% of Canadians were current smokers in 2012.¹² Three-quarters of these current smokers visited their doctor within the previous 12 months.¹² An American study with similar results (70% of smokers visited their doctor each year) established that 70-81% of these patients had an interest in quitting smoking, especially if they were in poor health.^{14,15} Unfortunately, for both countries, only half of these smokers report their doctor ever advising they quit smoking.^{12,14} Furthermore, only 61% of current smokers who were advised by their doctor to quit smoking ever received advice and information about quitting assistance.¹² The issue persists into specialty clinics for patients with advanced disease. Data from an ambulatory oncology centre revealed that 79% of patients were advised to quit smoking, and only 53% of these patients received specific recommendations on smoking cessation strategies.¹⁶ Eraker et al. reported that 50% of patients who quit smoking were influenced by their clinician indicating the important role health practitioners play in supporting smoking cessation.¹⁷

An estimated 25-80% of smokers will continue to smoke after a cancer diagnosis.^{6,11,18-20} This can have negative consequences on their health. For example, patients who are diagnosed with non-small cell lung cancer and who continue to smoke may double their risk of dying compared to those who quit.¹¹ A recent evidence review suggests that patients who quit smoking at the time of diagnosis may decrease their risk of dying by as much as 30-40%.³ In fact, the review concluded that for certain cancer diagnoses, these benefits may be equal to or exceed the benefits established by effective treatment modalities.³ Although nearly 69% of current smokers report a desire to quit after diagnosis, many will not be successful.³ In the short-term, highly motivated patients achieve a cessation rate of 70%, however relapse one to six months following cessation has been shown to occur in up to 50% of patients.³ Without proper evidence-based pharmacotherapy and counseling to support quit

attempts, abstinence is rare.³ Smoking cessation is an essential part of cancer treatment, however only 38% of treatment centers in the United States report smoking as a vital sign.^{3,21} The extent of reporting in Canada is unknown although the practice is highly recommended. Tobacco use must be tracked throughout comprehensive patient care, including consideration of factors associated with continued use.²² Heavy smokers, patients who are more nicotine dependent at the time of diagnosis, and those with lower levels of perceived risk are more likely to continue smoking.^{18,22} It can be difficult to quit, even for those who are highly motivated.²³ However, the increase in motivation and interest to quit smoking at diagnosis can be an excellent opportunity for healthcare providers to become involved in the quitting process.²⁴ Educating the patient about the importance of smoking cessation after a cancer diagnosis is necessary and will help patients to make informed decisions about improving their health.^{11,23} Most importantly, the message should be clarified that it is 'never too late to stop using tobacco'.²⁵

Unfortunately, attitudes prevail amongst health practitioners and patients that smoking cessation after a cancer diagnosis is useless and the risk remains underestimated.^{11,19} This is contrary to current evidence which links continued smoking to poorer outcomes.¹¹ Health practitioners can use a cancer diagnosis as a "teachable moment" for smoking cessation.⁶ Timing is crucial, as research has shown that motivation, receptive behaviour and success of smoking cessation treatments are higher the closer cessation occurs to diagnosis.^{5,6,26} Patients may have a variety of reasons to continue smoking.^{1,5,19-21,24,27} Regardless, they should be given a clear and consistent message regarding the importance of smoking cessation even if the cancer is not considered smoking-related or curable.⁶ Diagnosis is an optimal time to recommend smoking cessation because patients will have the benefit of personal support and encouragement from their healthcare team.²⁵

Mounting evidence strongly supports smoking cessation after a cancer diagnosis. Cancer patients who continue to smoke are at risk for poorer treatment outcomes, including decreased treatment effectiveness, decreased overall survival, increased risk of recurrence and metastases, and poorer quality of life.^{1-3,5,6,11,18-22,24-30} Several other studies have implicated continued smoking after a cancer diagnosis with increased risk of disease progression, increased morbidity, decreased safety of treatment modalities, impaired immune function, increased risk of infection, exacerbated drug toxicity, increased treatment complications, increased pain, impaired wound healing, development of second primary tumours, increased fatigue and poorer recovery.^{1-3,5,6,11,14,19,24-28} It has been emphasized that improved prognosis is possible with an increased interval between smoking cessation and the initiation of cancer treatment.²⁴ Adding to the benefits of smoking cessation after a cancer diagnosis are the benefits that patients can realize in other aspects of their health not associated with cancer (i.e., longer life span, improved lung function and reduced risk of heart disease).⁶

This guideline was initiated in response to variability in the message patients are receiving from their healthcare practitioners at CancerCare Manitoba regarding the impact of their smoking habits after a cancer diagnosis. Using evidence-based recommendations we hope to improve smoking abstinence whilst improving patient outcomes. This guideline focuses on reasons to support smoking cessation during the cancer journey; including the impact smoking has on an oncology patient's quality of life, treatment-related outcomes and treatment efficacy. Recommended treatment options for smoking cessation will be addressed in a separate guideline.

References

1. National Cancer Institute. Smoking in cancer care (PDQ®). National Institutes of Health, 2013. Updated August 2013. Available at: <http://cancer.gov/cancertopics/pdq/supportivecare/smokingcessation/HealthProfessional>. Accessed 22 April 2014.
2. Gritz ER. Smoking and smoking cessation in cancer patients. *Brit J Addict* 1991;86(5):549-54.
3. Toll BA, Brandon TH, Gritz ER. Assessing tobacco use by cancer patients and facilitating cessation: An American Association for Cancer Research policy statement. *Clin Cancer Res* 2013;19(8):1941-8.
4. Gritz ER, Dresler C, Sarna L. Smoking, the missing drug interaction in clinical trials: ignoring the obvious. *Cancer Epidem Biomar* 2005;14(10):2287-93.
5. Simmons VN, Litvin EB, Jacobsen PB, et al. Predictors of smoking relapse in patients with thoracic cancer or head and neck cancer. *Cancer* 2013;119(7):1420-7.
6. Garces YI, Schroeder DR, Nirelli LM, et al. Tobacco use outcomes among patients with head and neck carcinoma treated for nicotine dependence: a matched-pair analysis. *Cancer* 2004;101(1):116-24.
7. Lee PN & Forey BA. Indirectly estimated absolute lung cancer mortality rates by smoking status and histological type based on a systematic review. *BMC Cancer* 2013;13:189-225.
8. Dearing J. Disease-centered advice for patients with superficial transitional cell carcinoma of the bladder. *Ann R Coll Surg Engl* 2005;87(2):85-7.
9. Zeegers MP, Kellen E, Buntinx F, et al. The association between smoking, beverage consumption, diet and bladder cancer: a systematic literature review. *World J Urol* 2004;21(6):392-401.
10. Anderson B & Naish W. Bladder cancer and smoking. Part 1: Addressing the associated risk factors. *Brit J Nurs* 2008;17(18):1182-6.
11. Cataldo JK, Dubey S, Prochaska JJ. Smoking cessation: an integral part of lung cancer treatment. *Oncol* 2010;78(5-6):289-301.
12. Canadian Cancer Society. Smoking and tobacco. Updated 2014. Available at: <http://www.cancer.ca/en/prevention-and-screening/live-well/smoking-and-tobacco/?region=qc>. Accessed 15 August 2014.
13. Anderson B & Naish W. Bladder cancer and smoking. Part 3: Influence of perceptions and beliefs. *Brit J Nurs* 2008;17(20):1292-7.
14. Des Rochers C, Dische S, Saunders MI. The problem of cigarette smoking in radiotherapy for cancer in the head and neck. *Clin Oncol* 1992;4(4):214-6.
15. Browning KK, Ahijevych KL, Ross P, et al. Implementing the Agency for Health Care Policy and Research's Smoking Cessation Guideline in a lung cancer surgery clinic. *Oncol Nurs Forum* 2000;27(8):1248-54.

16. Cooley ME, Emmons KM, Haddad R, et al. Patient report of receipt and interest in smoking cessation interventions after a diagnosis of cancer. *Cancer* 2011;117(13):2961-9.
17. Eraker SA, Becker MH, Strecher VJ. Smoking behavior, cessation, techniques and the health decision model. *Am J Med* 1985;78(5):817-25.
18. Schnoll RA, James C, Malstrom M, et al. Longitudinal predictors of continued tobacco use among patients diagnosed with cancer. *Annals Behav Med* 2003;25(3):214-21.
19. Walker MS, Vidrine DJ, Gritz ER. Smoking relapse during the first year after treatment for early-stage non-small-cell lung cancer. *Cancer Epidem Biomar* 2006;15(12):2370-7.
20. Park ER, Japuntich SJ, Rigotti NA, et al. A snapshot of smokers after lung and colorectal cancer diagnosis. *Cancer* 2012;118(12):3153-64.
21. Hopenhayn C, Christian WJ, Christian A, et al. Factors associated with smoking abstinence after diagnosis of early stage lung cancer. *Lung Cancer* 2013;80(1):55-61.
22. Ostroff JS, Jacobsen PB, Moadel AB, et al. Prevalence and predictors of continued tobacco use after treatment of patients with head and neck cancer. *Cancer* 1995;75(2):569-76.
23. Anderson B & Naish W. Bladder cancer and smoking. Part 4: Efficacy of health promotion. *Brit J Nurs* 2008;17(21):1292-7.
24. Gritz ER, Fingeret MC, Vidrine DJ, et al. Successes and failures of the teachable moment: smoking cessation in cancer patients. *Cancer* 2006;106(1):17-27.
25. American Society of Clinical Oncology. Stopping tobacco use after a cancer diagnosis: resources and guidance for patients and families. Updated 2012. Available at: http://www.cancer.net/sites/cancer.net/files/stopping_tobacco_use.pdf. Accessed 22 April 2014.
26. American Society of Clinical Oncology. Tobacco cessation guide: for oncology providers. Updated 2012. Available at: http://www.asco.org/sites/default/files/tobacco_cessation_guide.pdf. Accessed 22 April 2014.
27. Cooley ME, Sarna L, Kotlerman J, et al. Smoking cessation is challenging even for patients recovering from lung cancer surgery with curative intent. *Lung Cancer* 2009;66(2):218-25.
28. Saskatchewan Cancer Agency. Smoking cessation in oncology: a practical guide for oncologists. Updated 2011. Available at: <http://www.saskcancer.ca/Practical%20Guide%20Oncologists%20May%2013>. Accessed on 22 April 2014.
29. Clark TG, Murphy MFG, Hey K, et al. Does smoking influence survival in cancer patients through effects on respiratory and vascular disease? *Eur J Cancer Prev* 2006;15(1):87-90.
30. Paleri V, Wight RG, Silver CE, et al. Comorbidity in head and neck cancer: a critical appraisal and recommendations for practice. *Oral Oncol* 2010;46(10):712-9.

II. Scope of Guideline

Aim and Purpose

Clinical Questions

In terms of a patient's quality of life during their cancer journey, is it important for an adult smoker to quit smoking after a cancer diagnosis?

In terms of a patient's treatment-related outcomes (survival, recurrence and second primary tumours), is it important for an adult smoker to quit smoking after a cancer diagnosis?

Is there a difference in treatment toxicity, treatment tolerance, and recovery during and after radiation therapy, chemotherapy or surgery in adult cancer patients who continue to smoke after a diagnosis compared to non-smokers?

Development Panel

Development Panel

| | |
|--|---|
| Nursing CancerCare Manitoba | 1 Nurse Practitioner 1 Nurse |
| Patient and Family Support Services CancerCare Manitoba | 1 Psychosocial Oncology Clinician |
| Pharmacy CancerCare Manitoba | 1 Pharmacist |
| Clinical Practice Guidelines Initiative CancerCare Manitoba | 1 Program Coordinator 1 Guidelines Analyst 1 Research Assistant |

Development Process

A small multidisciplinary working group participated in the development of this guideline. Recommendations were based on the best available evidence. All decisions were made using a modified Delphi consensus method (See Section III, Guideline Methodology, for description).

Patient Population and Healthcare Setting

The recommendations in this guideline are applicable to the care of adult (18 years or older; male or female) oncology patients who continue to smoke after a cancer diagnosis. These recommendations are intended for use in both inpatient and outpatient settings.

End-Users

This guideline is written for use by clinicians providing care for the above mentioned patient population. Intended primarily for use by medical clinicians, the guideline may be of interest to trainees, physician extenders, allied healthcare staff, healthcare administrators, policy-makers and possibly members of the general public.

III. Guideline Methodology

Clinical Research Question Development

The working group discussed several options for the focus of the present guideline. The topic revealed endless opportunities and it was decided that a series of guidelines would be developed based on the topic of smoking after a cancer diagnosis. The working group felt it was important to disseminate information about *why* it is important to quit smoking after a cancer diagnosis prior to providing information regarding *how* to quit smoking successfully. Continued discussion revealed several topics of interest within this narrowed scope. Discussion and consensus further narrowed the guideline down to three clinical research questions phrased using the PICO method (**P**opulation; **I**ntervention; **C**omparison; **O**utcome).

Clinical Question #1: In terms of a patient's quality of life during their cancer journey, is it important for an adult smoker to quit smoking after a cancer diagnosis?

Clinical Question #2: In terms of a patient's treatment related outcomes (survival, recurrence and second primary tumours), is it important for an adult smoker to quit smoking after a cancer diagnosis?

Clinical Question #3: Is there a difference in treatment toxicity, treatment tolerance and recovery during and after radiation therapy, chemotherapy or surgery in adult patients who continue to smoke after a cancer diagnosis compared to non-smokers?

Literature Search

Clinical Practice Guidelines

A preliminary search reviewed several clinical practice guideline databases to locate guidelines related to smoking cessation after a cancer diagnosis. These databases included CancerView: Standards and Guideline Evidence (SAGE), National Guideline Clearing House, Guidelines International Network (GIN), Canadian Medical Association (CMA), National Cancer Institute, American Cancer Society, New Zealand Guidelines Group, Scottish Intercollegiate Guidelines Network (SIGN), National Institute for Health and Care Excellence (NICE), American Society of Clinical Oncology (ASCO), BC Cancer Agency, Alberta Health Services, Saskatchewan Cancer Agency, Cancer Care Ontario, Ontario Medical Association and Cancer Care Nova Scotia. Several guidelines are available which focus on smoking-related cancers and smoking cessation treatment options for cancer patients; however, the search yielded no current guidelines related to *why* smoking cessation is important after a cancer diagnosis. Therefore, adaptation of a guideline for CancerCare Manitoba was not an option as there were no guidelines addressing our clinical research questions.

Although no existing clinical practice guidelines were found to support our questions of interest, Saskatchewan Cancer Agency and ASCO have developed useful online resources for patients and providers listing several reasons to quit smoking after a cancer diagnosis. These guides were integrated into our guideline development.

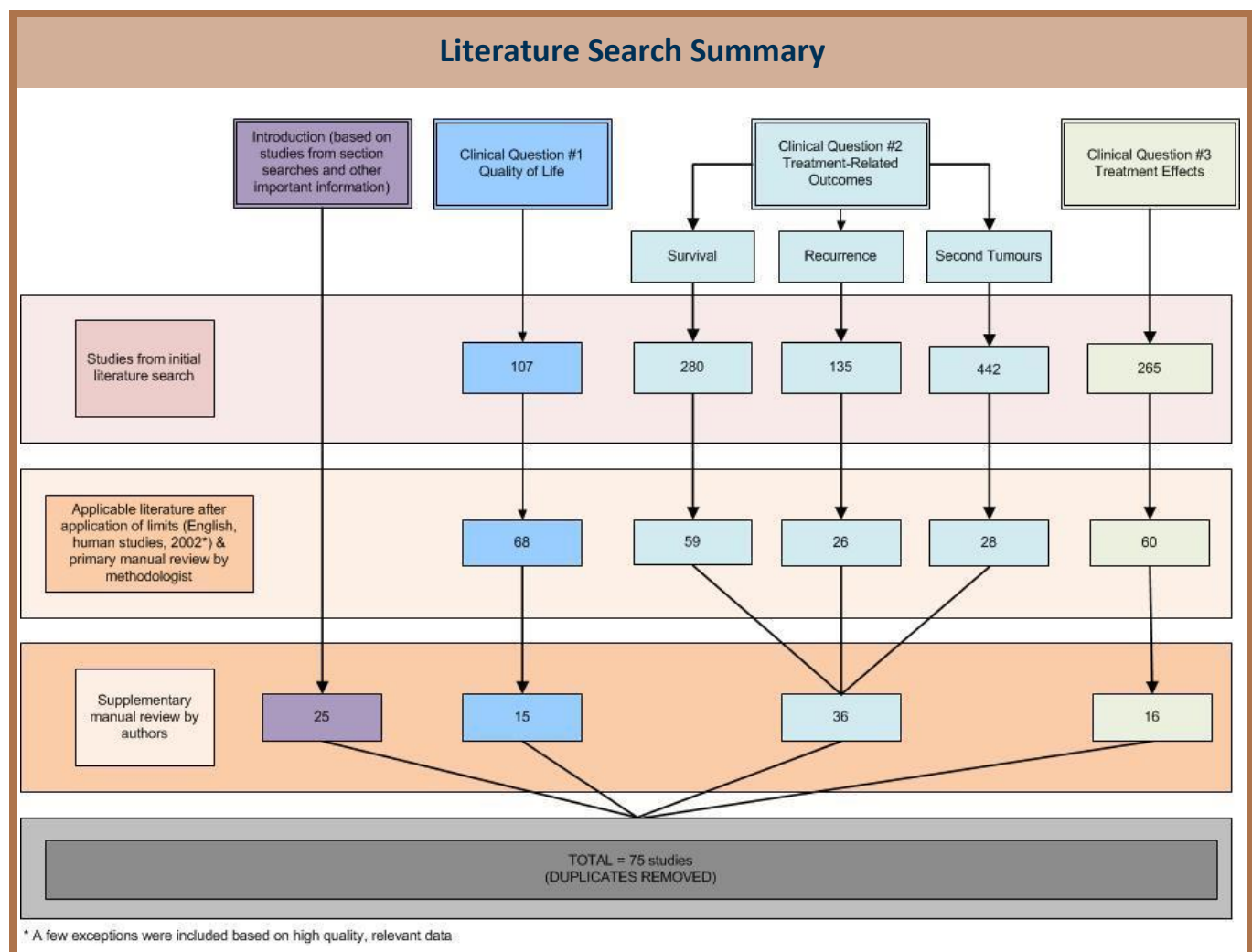
Literature Review of Primary Evidence

A preliminary search conducted in March 2013 via PubMed identified and refined keywords. This included terms and relevant synonyms reflecting concepts of quality of health, treatment-related outcomes (survival, recurrence and second primary tumours) and treatment responses (toxicity, tolerance and recovery) in patients who continue to smoke after a cancer diagnosis. After terms were defined, a literature search was systematically completed using five electronic databases (PubMed, OVIDsp, Cochrane Reviews, Clinical Trials.gov, CINAHL/EBSCOHOST) between April and June of 2013. Separate literature reviews were completed for the three clinical research questions. Combinations of the keywords shown in Table 1 were used for these searches. Identification of additional articles was completed using a snowballing technique, which involved moving backwards by following references of eligible papers and forward through citation chasing. Environmental searches of Google and Google Scholar were completed but were of limited value.

Literature Review Search Terms

| Clinical Research Question | Search Terms |
|----------------------------|--|
| Quality of Life | (MESH = Neoplasms OR TI/AB = cancer OR tumor OR tumors OR tumour OR tumours OR malignancy OR malignant) AND (TIAB = diagnosis OR post-diagnosis OR post diagnosis OR postdiagnosis OR after diagnosis) AND (MESH = smoking OR TIAB = tobacco use OR tobacco user OR cigarette OR cigarettes OR tobacco smoker OR smoke) AND (MESH = Quality of Life OR TIAB = QOL). |
| Treatment-Related Outcomes | (MESH = Neoplasms OR TI/AB = cancer OR tumor* OR tumour* OR malignancy OR malignant) AND (TIAB = diagnosis OR post-diagnosis OR post diagnosis OR postdiagnosis OR after diagnosis) AND (MESH = smoking OR TIAB = tobacco use OR tobacco user OR cigarette OR cigarettes OR tobacco smoker OR smoke) AND [(MESH = Survival OR Disease-Free Survival OR Mortality OR TIAB = DFS OR OS) OR (MESH = recurrence OR TIAB = Relapse OR Reoccurrence) OR (MESH = Neoplasm Metastasis OR MESH subheading = secondary OR TIAB = metastatic OR metastases OR metastasis) |
| Treatment Effects | (MESH = Neoplasms OR TI/AB = cancer OR tumor OR tumors OR tumour OR tumours OR malignancy OR malignant) AND (TIAB = diagnosis OR post-diagnosis OR post diagnosis OR postdiagnosis OR after diagnosis) AND (MESH = smoking OR TIAB = tobacco use OR tobacco user OR cigarette OR cigarettes OR tobacco smoker OR smoke) AND (MESH = Radiotherapy OR Chemoradiotherapy, OR General Surgery OR Chemotherapy Adjuvant OR TIAB = Radiation Therapy OR Chemoradiation OR Surgery OR Surgical OR cancer treatment OR chemo OR RT) AND (MESH = Drug toxicity OR MESH Subheading = toxicity OR adverse effects OR TIAB = tolerance OR treatment tolerance OR side effects OR side-effects OR recovery OR treatment toxicity OR toxicity) |

Findings for literature supporting each clinical research question were as follows: Clinical Research Question 1 (Quality of Life) = 107; Clinical Research Question 2 (Treatment-Related Outcomes) broken down into Survival = 280, Recurrence = 135 and Second Primary Tumours = 442; Clinical Research Question 3 (Treatment Effects) = 265. Limiting the search to literature on humans, in English and published after 2002 reduced the number of papers fitting our selection criteria. There were a few exceptions to the 2002 cut-off based on high quality, relevant data. All titles and available abstracts were downloaded and reviewed for quality, connection, accessibility and redundancies. Selection criteria and review reduced applicable literature for each research question to: Clinical Research Question 1 (Quality of Life) = 68; Clinical Research Question 2 (Treatment-Related Outcomes) broken down into Survival = 59, Recurrence = 26 and Second Primary Tumours = 28; Clinical Research Question 3 (Treatment Effects) = 60. Finally, selected literature was read, summarized and grouped according to theme and level of evidence. A supplementary manual review was conducted by authors as they drafted their sections. A total of seventy-five quality articles were included in this guideline.



Working Group Meetings

Each guideline section was drafted by the working group members based on the best available evidence. The sections were reviewed and amended at each working group meeting based on consensus decisions (*See Section X for working group members*).

Internal and External Review

Internal and external peer reviews were pursued, the results of which are appended to these guidelines. The internal review process was consensus-based and completed by the working group. An external review was conducted by a nurse practitioner from the Alberta Thoracic Oncology Program/Chest Medicine Clinic, the cancer prevention coordinator from Cancer Care Nova Scotia, a family practitioner in oncology from CCMB and a medical oncologist from CCMB (*See Section X*). All reviewers completed a full review of the guideline document and submitted a standardized practitioner feedback survey (adapted from Brouwers and colleagues).¹ All feedback was considered and discussed by the working group. Decisions to incorporate any changes into the guideline were consensus-based (acceptance, rejection or acceptance with modifications).

Maintenance

Clinical practice guidelines are considered 'living' documents which require ongoing evaluation, review and update. Re-evaluation of this guideline is planned for 2017. The working group will revise and update the document as needed, with any critical new evidence brought forward before this scheduled review.

References

1. Brouwers MC, Graham ID, Hanna SE, et al. Clinicians' assessments of practice guidelines in oncology: the CAPGO survey. *Int J Technol Assess Health Care* 2004;20(4):421-6.

IV. Quality of Life

Background

Cigarette smoking is recognized as contributing to the development of cancer and adversely impacting quality of life among patients who continue to smoke during and after treatment.^{1,2} Quality of life is a multidimensional state of being that includes physical, functional, psychological and social well-being of one's self.³ A patient's quality of life prior to their cancer treatment is known to be a strong predictor of survival and toleration of treatment.⁴ Furthermore, progress in the treatment and management of cancer has led to extended life expectancy for many patients, including those diagnosed with lung cancer, leading to consideration of quality of life as an important factor in both immediate and long-term contexts.⁵

Studies examining the impact of smoking cessation with respect to cancer patients' quality of life have consistently shown benefits for patients who quit smoking. Key evidence, as discussed below, shows improvements with respect to patients' mental health, cognitive function and performance status, as well as, reduced symptom burden.^{2,6-8} These study findings parallel similar evidence gathered in smoking cessation studies conducted in the general population.⁸⁻¹⁰

Key Evidence

A growing body of evidence shows that smoking is an important variable to consider in relation to quality of life for cancer patients. Evidence shows that continuing to smoke after a cancer diagnosis has a negative impact on patients' quality of life, while quitting smoking contributes to improved quality of life.¹ For example, Myrdal et al. conducted a post-treatment comparative study regarding the experiences of patients with primary non-small cell bronchogenic carcinoma of the lung.⁶ Quality of life data was gathered using the short form-36 (SF-36) instrument, which is designed to evaluate health related quality of life in various groups of patients along 8 dimensions. The evidence revealed that those who continued to smoke after surgery (n = 13) had significantly lower scores for mental health (p = 0.003), vitality (p = 0.027) and the mental components summary (p = 0.003) compared to those who stopped smoking at, or prior to surgery (n = 72) and those who had never smoked (n = 21).

Similarly, Humphris and Rogers conducted a longitudinal study which examined the role of psychosocial factors in relation to smoking behaviours over 12 months with a consecutive group of head and neck cancer patients (n=87) attending a regional treatment unit.¹¹ Psychological distress data was gathered using self-reported measures including the Hospital Anxiety and Depression Scale (HADS). The results showed that smokers (n = 20) had a significantly raised level of distress (anxiety: p < 0.001; depression: p < 0.05) at each assessment after the baseline, compared to those who abstained (n = 37; 10 were non-smokers and 27 had a previous smoking history).

Evidence related to quality of life indicators that include cognitive function, performance status and symptom burden also reveals support for the benefits of quitting smoking at time of diagnosis. In a retrospective review, Baser et al. compared the records of patients with non-small cell lung cancer (NSCLC) who had been referred for

evaluation of surgical resectability, on the basis of performance status (PS) and survival over a 12 month period.⁷ The study sample (n = 206) included 93 current smokers, of whom 46 quit smoking and 47 continued smoking after diagnosis (otherwise similar on other variables such as disease stage, demographics, treatment modalities and comorbidities). While no significant association between smoking status after diagnosis and patient survival was found, those who quit smoking maintained a better PS at 0 to 6 months (p = 0.002) and at 0 to 12 months (p = 0.006) than those who continued to smoke (p = 0.1786).

Similar findings in the head and neck cancer population were found by Jensen et al. Participants in this Danish study were consecutive, recurrence free patients being seen in follow-up after being treated with radical radiotherapy or surgery for larynx, pharynx or oral cavity cancer. They completed quality of life self-report instruments (European Organization for Research and Treatment of Cancer (EORTC) quality of life questionnaires (QLQ), C30 and H & N35) and were assessed for WHO Performance Status.² When results were compared on the basis of smoking status, the difference was significant. Participants who were smokers at follow-up had the lowest function scores and the highest symptom scores in the EORTC QLQ, except for fibrosis and weight gain. Significant differences were shown on 20 of the 33 quality of life scales of the EORTC QLQ (p < 0.05) with cognitive function, nausea/vomiting, dyspnoea, appetite loss, diarrhea and weight loss statistically significant (p < 0.005). Participants who had been smokers prior to diagnosis and had quit had quality of life scores between those of “never smokers” and those who continued to smoke (Table 1).

It is notable that the large prospective cohort study (n = 1028) by Garces and colleagues attained similar evidence in studying the relationship between cigarette smoking status and quality of life among lung cancer survivors. These researchers used the lung cancer symptom scale (LCSS), in which lower scores correspond to a better quality of life.⁸ The adjusted mean scores showed that a significant separation (p < 0.0001) between never-smokers (mean = 17; standard deviation [SD], 4.02) and persistent smokers (mean = 28.7; SD, 5.09), with abstinent smokers (mean = 22.1; SD, 4.03) situated midway on the continuum between the two groups. Thus, never-smokers reported the best quality of life, while abstinent smokers reported a better quality of life relative to persistent smokers who reported the worst quality of life on every variable measured, as illustrated by Table 1.

Table 1. Quality of Life

| Author | Quality of Life Measure | Never Smoker Mean (SD) N = 14 | Quitters [‡] Mean (SD) N = 48 | Current Smoker Mean (SD) N = 52 |
|----------------------------|--------------------------|--------------------------------------|---|---------------------------------------|
| Jensen et al. ² | Physical Function | 98 | 83 | 78 |
| | Cognitive Function | 94 | 88 | 73 |
| | Nausea/Vomiting | 0 | 3 | 14 |
| | Dyspnoea | 0 | 9 | 22 |
| | Diarrhea | 7 | 8 | 23 |
| | Appetite Loss | 7 | 13 | 38 |
| | Weight Loss | 0 | 10 | 37 |
| Garces et al. ⁸ | | Never Smoker Mean (SD) N = 180 | Abstinent Smoker [‡] Mean (SD) N = 173 | Current Smoker Mean (SD) N = 75 |
| | Appetite* | 16.1 (4.88) | | 26.1 (5.57) |
| | Fatigue* | 31.0 (5.14) | | 44.4 (6.24) |
| | Coughing* | 17.5 (4.53) | | 34.5 (5.66) |
| | Dyspnoea* | 23.4 (4.50) | | 37.0 (5.96) |
| | Hemoptysis | 1.6 (0.81) | | 5.2 (1.27) |
| | Pain | 8.8 (2.07) | | 16.2 (2.53) |
| | Symptomatic Distress* | 8.8 (3.46) | | 19.1 (5.34) |
| | Effect on Activities* | 14.7 (5.53) | | 26.6 (7.84) |
| | Overall Quality of Life* | 17.4 (6.35) | | 31.1 (8.03) |
| | LCSS Total Score* | 17.6 (4.02) | 22.1 (4.03) | 28.7 (5.09) |

*Indicates statistically significant difference between never smokers and current smokers (p < 0.001)

[‡]A Quitter is defined as an individual who was a smoker at diagnosis but became abstinent from smoking at the time of follow-up, and those who were former smokers at diagnosis and maintained cessation at follow-up.

[‡]An Abstinent Smoker is defined as an individual who was a smoker at diagnosis but became abstinent from smoking at the time of follow-up. Note: data for quality of life measures of this subgroup were not available.

Abbreviations: LCSS, lung cancer symptom scale; N, sample size; SD, standard deviation

The aforementioned evidence demonstrates that cancer patients who stop smoking and abstain after their diagnosis and treatment have improved quality of life, as well as prolonged survival.¹⁵ This can have indirect positive effects on the motivation of family members to quit smoking and improve their own health.¹⁵

Patients who are anxious or stressed may be at highest risk of continuing to smoke after a diagnosis.¹⁶ Neurocognitive addiction is understood and reflected in the higher rates of smoking. This means that cancer patients who experience anxiety should have regular and consistent smoking cessation support after treatment. In fact, patients with smoking related cancers who experience symptoms of anxiety or depression should be treated for their psychological distress to prevent smoking relapse.¹³

History of major depression is positively related to smoking initiation and intensity; however, depressive symptoms sometimes remain undetected in cancer patients.¹⁷ Depressed smokers are 40% less likely to quit smoking compared to non-depressed smokers (relative risk, 0.6; $p < 0.05$).¹⁸ Addressing depression is a critical aspect of effective smoking cessation programming among cancer survivors.¹³ The negative stigma smoking carries is known to be strongly correlated with depression and a decrease in a patient's quality of life.¹⁴ Treating depression and smoking more aggressively is likely to improve quality of life.¹⁷ Furthermore, smoking cessation has been shown to improve cognitive function and self-esteem.⁵ Therefore, counseling, support and education regarding anxiety management and smoking cessation coping strategies should be considered essential elements in the care of cancer patients who wish to quit smoking.

Recommendations

1. To improve quality of life, patients with any type of cancer should be encouraged to quit smoking at any point in their journey by their oncologists and by other oncology team members.
2. Clinicians should approach quality of life discussions with patients and family members taking into consideration patient context, patient environment and cultural norms of practices, which are important factors to include in smoking cessation strategies. *Level of Evidence IV*
3. Counseling and education regarding anxiety management and smoking cessation coping strategies should be incorporated into the care of cancer patients.

References

1. Duffy SA, Terrell JE, Valenstein M, et al. Effect of smoking, alcohol, and depression on quality of life of head and neck cancer patients. *Gen Hosp Psychiatry* 2002;24(3):140-7.
2. Jensen K, Jensen AB, Grau C. Smoking has a negative impact upon health related quality of life after treatment for head and neck cancer. *Oral Oncol* 2007;43(2):187-92.
3. Gritz ER, Carmack CL, de Moor C, et al. First year after head and neck cancer: quality of life. *J Clin Oncol* 1999;17(1):352-60.
4. Browning KK, Ferketich AK, Otterson GA, et al. A psychometric analysis of quality of life tools in lung cancer patient who smoke. *Lung Cancer* 2009;66(1):134-9.

5. Cataldo JK, Dubey S, Prochaska JJ. Smoking cessation: an integral part of lung cancer treatment. *Oncol* 2010;78(506):289-301.
6. Myrdal G, Valtysdottir S, Lambe M, et al. Quality of life following lung cancer surgery. *Thorax* 2003;58(3):194-7.
7. Baser S, Shannon VR, Eapen GA, et al. Smoking cessation after diagnosis of lung cancer is associated with a beneficial effect on performance status. *Chest* 2006;130(6):1784-90.
8. Garces YI, Yang P, Parkinson J, et al. The relationship between cigarette smoking and quality of life after lung cancer diagnosis. *Chest* 2004;126(6):1733-41.
9. Stewart AL, King AC, Killen JD, et al. Does smoking cessation improve health-related quality-of-life? *Ann Behav Med* 1995;17(4):331-8.
10. Croghan IT, Schroeder DR, Hays JT, et al. Nicotine dependence treatment: perceived health status improvement with 1-year continuous smoking abstinence. *Eur J Public Health* 2005;15(3):251-5.
11. Humphris GM & Rogers SN. The association of cigarette smoking and anxiety, depression and fears of recurrence in patients following treatment of oral and oropharyngeal malignancy. *Eur J Cancer Care* 2004;13(4):328-35.
12. Simmons VN, Litvin EB, Jacobsen PB, et al. Predictors of smoking relapse in patient with thoracic cancer or head and neck cancer. *Cancer* 2013;119(7):1420-7.
13. Berg CJ, Thomas AN, Mertens AC, et al. Correlates of continued smoking vs. cessation among survivors of smoking-related cancers. *Psycho-Oncology J* 2012;22(4):799-806.
14. Cataldo JK, Jahan TM, Pongquan VL. Lung cancer stigma, depression and quality of life among ever and never smokers. *Eur J Oncol Nurs* 2012;16(3):264-9.
15. Gritz ER, Fingeret MC, Vidrine DJ, et al. Successes and failures of the teachable moment: smoking cessation in cancer patients. *Cancer* 2006;106(1):17-27.
16. Dean GE, Dean GE, Finnell DS, Scribner M, et al. Sleep in lung cancer: the role of anxiety, alcohol and tobacco. *J Addict Nurs* 2010;21(2-3):130-8.
17. Duffy SA, Ronis DL, Valenstein M, et al. The University of Michigan Head and Neck Cancer Team. Depressive symptoms, smoking, drinking, and quality of life among head and neck cancer patients. *Psychosomatics* 2007;48(2):142-8.
18. Anda RF, Williamson DF, Escobedo LG, et al. Depression and the dynamics of smoking. A national perspective. *JAMA* 1990;264(12):1541-5.

V. Treatment-Related Outcomes

Background

There is widespread agreement in the literature to support the importance of an adult smoker quitting smoking after a cancer diagnosis. Benefits are seen across many types and stages of cancer. Treatment-related outcomes are improved, with respect to relapse/recurrence, survival and development of second primary tumours, when smokers quit after diagnosis. Furthermore, evidence continues to mount regarding the adverse effects of continued smoking after a diagnosis of cancer, specifically, “substantial adverse effects on treatment effectiveness, overall survival, risk of second primary malignancy, and quality of life”.¹

The time of diagnosis is a ‘window of opportunity’ for healthcare providers to engage patients in smoking cessation efforts.² It is important to take these opportunities to motivate patients to quit smoking, as they are often interested in quitting after a cancer diagnosis.² The evidence clearly supports the benefits of intervening and assisting in a patient’s quitting process as early as possible.² Evidence suggests, “that the risk of dying could be lowered by 30-40% by quitting smoking at the time of diagnosis. For some cancer diagnoses, the benefit of smoking cessation may be equal to, or even exceed, the value of state-of-the-art cancer therapies.”¹³ Key evidence, as discussed below, supports the necessity of smoking cessation after a cancer diagnosis with respect to relapse/recurrence, survival and second primary tumours.

Key Evidence

Relapse / Recurrence

Evidence shows that those who stop smoking after diagnosis have a better chance of successful treatment, whereas, those who continue to use tobacco face the risk of increased chance of recurrence.⁴ This is particularly well documented in early stage lung cancer studies. Parsons et al. conducted a systematic review with meta-analysis which revealed improved prognostic outcomes in patients who abstained from smoking after diagnosis with early stage NSCLC compared to those who continued to smoke (hazard ratio [HR] for risk of recurrence, 1.26; 95% CI, 1.06-1.50).⁵ Furthermore, patients who continued to smoke after diagnosis more than doubled their risk of dying (HR for all-cause mortality, 2.94; 95% CI, 1.15-7.54). By way of contrast, those who chose smoking cessation realized significant health benefits. Illustrative of this, Gritz et al. reiterate that “smoking cessation at the time of diagnosis of lung cancer may reduce the rate of development of metachronous tumours”.⁶ Based upon this and many other findings, these researchers advocate for smoking cessation programming as a critical component of care in the treatment of lung cancer. Similarly, Chen et al. found that patients diagnosed with head and neck cancer who quit smoking prior to radiation therapy compared to those who continued to smoke had superior five-year overall survival rates (55% versus 23%; $p < 0.05$), locoregional control (69% versus 58%; $p < 0.05$) and disease-free survival (65% versus 42%; $p < 0.05$).⁷

Evidence also indicates that patients who quit smoking are less likely to experience relapse or recurrence of their cancer than those who continue to smoke. This is well demonstrated by the findings of Joshu et al. in their study of a cohort of 1416 men who had undergone radical prostatectomies with the same surgeon and were followed

for a mean of 7.3 years.⁸ They found that the cohort showed recurrence rates of 34.3% for current smokers, whereas former smokers, those who had quit within the first year after surgery, had a recurrence rate of 14.8%.⁸ Chen et al. found similar evidence for patients diagnosed with nonmuscle-invasive bladder cancer where quitters (stopped smoking within a year before and three months after the diagnosis) showed a recurrence-free survival rate of 70% compared to those who continued to smoke, at 45%, upon their three year follow-up.⁹ It was concluded that cancer recurrence and overall mortality may be significantly reduced if bladder cancer patients quit smoking at the time of diagnosis.^{9,10}

While considerable evidence regarding the impact of smoking cessation upon relapse and recurrence rates is available from lung cancer studies, the availability of such strong evidence from studies of other disease sites further reinforces the efficacy of smoking cessation as a potent treatment consideration.

Survival

Overall survival is proven to be negatively impacted by continued smoking. Researchers emphasize that smoking pack-years provides prognostic value of overall long-term survival in patients.¹² Substantial research has shown that for patients being treated for cancer, quitting smoking is associated with longer survival.^{4,13}

Zhou et al. conducted a cohort study in early stage NSCLC patients evaluating the benefit of smoking cessation on overall survival. Patients were analyzed based on their smoking status and number of years since cessation.¹⁴ The 5-year overall survival rates were 50% for current smokers, 76% for never smokers, 54% for ex-smokers who quit 1-8 years, 59% for ex-smokers who quit 9-17 years, and 58% for ex-smokers who quit \geq 18 years prior to diagnosis ($p = 0.09$, log-rank test). The adjusted hazard ratios significantly decreased the longer the time since cessation when compared with current smokers ($p = 0.004$). This data indicates an association between improved survival and time since cessation.¹⁴ These conclusions are further corroborated by a retrospective review conducted by Videtic and colleagues that compared patients with limited stage small cell lung cancer (LSCLC) who continued to smoke during chemotherapy and radiation therapy, to those who did not smoke.¹¹ They found that patients who continued to smoke had poorer survival compared to former smokers (13.6 versus 18 months).¹¹ Furthermore, studies have substantiated the continued benefit of smoking cessation for lung cancer patients irrespective of surgical and treatment timing.^{15,16} Improved overall survival after smoking cessation is also seen in mesothelioma, patients undergoing hematopoietic stem cell transplant for the treatment of acute leukemia, and acute myeloid leukemia (AML).¹⁷⁻¹⁹ Conversely, other studies support that smoking at the time of treatment for lung cancer has a significant negative effect on overall survival.^{20,21}

Research specific to gynecological malignancies indicates that when women are treated with chemoradiation for locally advanced cervical cancer, smoking predicts worse overall survival.¹² Notably, a study of patients with ovarian cancer found that for every 5 years since quitting smoking there was an 11% decrease in risk of ovarian cancer death (HR, 0.89; 95% CI, 0.94-1.15).²² In 1993, it was established that smoking was an independent predictor of survival for those being treated with head and neck cancer.²³ In patients with prostate cancer, Gong et al. conducted a case-control study ($n = 752$) which demonstrated that smokers in comparison to never smokers had a 2.66 relative hazard of prostate cancer-specific death ($p = 0.03$).²⁴ In fact, research has shown that when prostate cancer patients were abstinent from smoking for 10 years or longer, they had similar mortality rates to that of non-smokers.²⁵

Cancer progression has been shown to be significantly affected by smoking. A systematic review completed by Parsons et al. illustrates that there can be significant improvements in prognostic outcomes in patients with early stage lung cancer who have successfully quit smoking.⁵ Their research further proposes that much of this gain is due to reduced cancer progression.⁵ In patients with anal carcinoma, tobacco smoking was associated with a non-significant trend in disease recurrence (32% of smokers versus 20% of non-smokers with recurrence; $p = 0.17$) and a significant increase in mortality 5 years after treatment (45% of smokers versus 20% of non-smokers; $p = 0.05$).²⁶ This effect was also seen in a retrospective cohort study of men who underwent prostatectomies and continued to smoke at one year after surgery.⁸ Compared to never smokers, these patients were more likely to experience disease recurrence (HR, 2.31; 95% CI, 1.05 to 5.10).⁸ Gillison et al. concluded that the “risk of oropharyngeal cancer progression and death increases directly as a function of tobacco exposure at diagnosis and during therapy and is independent of tumor p16 status and treatment”.²⁷

Long-term treatment toxicity is also a consideration for survival. Smoking cessation has been found to be an important aspect in the prevention of certain long-lasting symptoms after radiotherapy.²⁸ Furthermore, research has shown that recovery can be detrimentally impacted by continued smoking after diagnosis and during treatment. Balduyck et al. have found that patients who continue to smoke will not return to their previous baseline physical, social function, or role, such as work, household activities and hobbies, after surgery by their 12 month follow-up.²⁹

Second Primary Tumours

It is widely accepted that patients who survive initial cancers are at increased risk for second primary tumours due to risk factors including smoking, alcohol use, radiation and chemotherapy. Evidence supports smoking cessation as a valuable intervention to decrease the risk of second primary tumours.

History of smoking is a universally accepted risk factor for second malignancy in patients diagnosed with head and neck squamous cell carcinoma (HNSCC) as their primary cancer. Many cross-sectional investigations have shown a cumulative effect of intense smoking on cancer.³⁰ One longitudinal study evaluated the patterns of smoking for over 10 years following a HNSCC diagnosis and found that those who were smokers at the time of diagnosis were three times more likely to develop a second smoking-related cancer, compared to those who never smoked.³⁰ However, former smokers and recent quitters who abstained from smoking were only 1.5 times more likely to develop a second primary cancer compared to never smokers, although this difference was not statistically significant.³⁰ The rate of developing a second primary tumour decreased relative to the smoking status at time of randomization, as demonstrated in the table below. Current smokers also had the lowest Kaplan-Meier estimate of second primary tumour-free survival (Table 2).³⁰

Table 2. Relation between Smoking Status and Rate of Developing Second Primary Tumours³⁰

| Group | Group Definition | Rate of Developing a Second Primary Tumour |
|-----------------|--|--|
| Current Smokers | Patients who continued to smoke at the time of randomization | 22% |
| Recent Quitters | Patients who quit smoking less than 12 months before randomization | 14.5% |
| Former Smokers | Patients who quit smoking more than 12 months before randomization | 13.2% |
| Never Smokers | Patients who have smoked less than 100 cigarettes or 5 packs in their lifetime | 8.8% |

A supporting study by Garces et al. suggests that patients with head and neck cancer can decrease their risk of developing a smoking-related second primary tumour by abstaining from tobacco use.³¹ Additional research suggests that there is a significantly higher risk of developing a smoking-related second primary tumour if patients continue to smoke after treatment for head and neck cancer. In one study, Do et al. indicated that continuing to smoke after a diagnosis of HNSCC may be a more serious risk factor than an intense smoking history prior to the diagnosis.³²

Continuing to smoke after being treated for small-cell lung carcinoma (SCLC) increases the risk of developing a second aerodigestive cancer. There is also evidence that continued smoking may influence the time to development of these cancers. In a retrospective review, Richardson et al. found a four-fold reduction in relative risk of second primary lung cancers at 10 years when comparing patients who continued to smoke and those who quit.³³

Other data supports these results, revealing that the overall risk of developing a second lung cancer is approximately double in those who continue to smoke. The lowest risk of developing a second lung cancer was seen in those who quit prior to diagnosis of SCLC.²⁰ Intensity of smoking (pack-years smoked prior to diagnosis) did not affect the risk, but when comparing patients of similar smoking intensity, the risk of second cancer was higher in those who continued to smoke.²⁰

When treated with radiotherapy, patients diagnosed with Hodgkin’s disease have an increased risk of developing lung cancer due to the dose of radiotherapy received in the lung area. Research has shown that radiation and smoking positively interact to exponentially increase the carcinogenic effects of *both* smoking and radiation. Those who did not smoke after diagnosis had a decreased risk of lung cancer, compared with those who continued to smoke after a Hodgkin’s diagnosis.³⁴ Moderate to heavy smoking greatly increases the risk of developing lung cancer after receiving treatment for Hodgkin’s. Table 3 shows the corresponding rates of lung cancer development in Hodgkin’s patients due to the effects of treatment, smoking and a combination of the two.

Table 3. Effects of Smoking on the Development of Second Primary Tumours in Hodgkin's Patients³⁵

| Group | Rate of Developing Second Primary Tumour |
|--------------------------------|--|
| Treatment Alone | 9.6% |
| Smoking Alone | 24.1% |
| Treatment and Smoking Combined | 63.3% |

One study found that although there was an increased risk for second primary tumours in smokers with gastric cancer, there was no increased risk seen in ex-smokers compared with non-smokers.³⁶ This provides a compelling incentive for smokers with gastric cancer to quit.³⁶

Recommendation

1. Adult smokers should quit smoking after a cancer diagnosis. Evidence suggests that those who quit will have improved prognosis, lower relapse/recurrence rates and fewer second primary tumours.

References

1. Gritz ER, Fingeret MC, Viidrine DJ, et al. Successes and failures of the teachable moment: smoking cessation in cancer patients. *Cancer* 2006;106(1):17-27.
2. Gritz ER, Dresler C, Sarna L. Smoking, the missing drug interaction in clinical trials: ignoring the obvious. *Cancer Epidem Biomar* 2005;14(10):2287-93.
3. Toll BA, Brandon TH, Gritz ER, et al. Assessing tobacco use by cancer patients and facilitating cessation: an American Association for Cancer Research policy statement. *Clin Cancer Res* 2013;19(8):1941-8.
4. American Society of Clinical Oncology. Stopping tobacco use after a cancer diagnosis: Resources and guidance for patients and families. Updated 2012. Available at: http://www.cancer.net/sites/cancer.net/files/stopping_tobacco_use.pdf. Accessed 22 April 2014.
5. Parsons A, Daley A, Begh R, et al. Influence of smoking cessation after diagnosis of early stage lung cancer on prognosis: Systematic review of observational studies with meta-analysis. *Br Med J* 2010;340:b5569.
6. Gritz ER, Vidrine DJ, Lazev AB. Smoking cessation in cancer patients: never too late to quit. In: C.W. Green, B. Given, V.L. Champion, S. Kozachik, D.N. Devoss (Eds.), *Evidence-based cancer care and prevention: Behavioral interventions* (pp. 107-40). New York: Springer Publishing Company, 2003.

7. Chen J, Chen LM, Vaughan A, et al. Tobacco smoking during radiation therapy for head-and-neck cancer is associated with unfavorable outcome. *Int J Radiat Oncol Biol* 2011;79(2):414-9.
8. Joshi CE, Mondul AM, Meinhold CL, et al. Cigarette smoking and prostate cancer recurrence after prostatectomy. *J Natl Cancer Inst* 2011;103(10):835-8.
9. Chen C, Shun C, Huang K, et al. Stopping smoking might reduce tumour recurrence in nonmuscle-invasive bladder cancer. *BJU Intl* 2007;100(2):281-6.
10. Saskatchewan Cancer Agency. Smoking cessation in oncology: a practical guide for oncologists. Updated 2011. Available at: <http://www.saskcancer.ca/Practical%20Guide%20Oncologists%20May%2013>. Accessed on 22 April 2014.
11. Videtic MM, Stitt LW, Dar AR, et al. Continued cigarette smoking by patients receiving concurrent chemoradiotherapy for limited-stage small-cell lung cancer is associated with decreased survival. *J Clin Oncol* 2003;21(8):1544-9.
12. Fujisawa T, Iizasa T, Saitoh Y, et al. Smoking before surgery predicts poor long-term survival in patients with stage I non-small-cell lung carcinomas. *J Clin Oncol* 1999;17(7):2086-91.
13. Ferketich AK, Niland JC, Mamet R, et al. Smoking status and survival in the National Comprehensive Cancer Network non-small cell lung cancer cohort. *Cancer* 2013;119(4):847-53.
14. Zhou W, Suk Heist R, Liu G, et al. Smoking cessation before diagnosis and survival in early stage non-small cell lung cancer patients. *Lung Cancer* 2006;53(3):375-80.
15. Sardari Nia P, Weyler J, Colpaert C, et al. Prognostic value of smoking status in operated non-small cell lung cancer. *Lung Cancer* 2005;47(3):351-9.
16. Mason DP, Subramanian S, Nowicki ER, et al. Impact of smoking cessation before resection of lung cancer: a society of thoracic surgeons general thoracic surgery database study. *Annals Thorac Surg* 2009;88(2):362-71.
17. Flores RM, Zakowski M, Venkatraman E, et al. Prognostic factors in the treatment of malignant pleural mesothelioma at a large tertiary referral center. *J Thorac Oncol* 2007;2(1):957-65.
18. Ehlers SL, Gastineau DA, Patten CA, et al. The impact of smoking on outcomes among patients undergoing hematopoietic stem cell transplant for the treatment of acute leukemia. *Bone Marrow Transpl* 2011;46(2):285-90.
19. Varadarajan R, Licht AS, Hyland AJ, et al. Smoking adversely affects survival in acute myeloid leukemia patients. *Intl J Cancer* 2012;130(6):1451-8.
20. Tucker MA, Murray N, Shaw EG, et al. Second primary cancers related to smoking and treatment of small-cell lung cancer. *J Natl Cancer Inst* 1997;89(23):1782-8.
21. Tammemagi CM, Neslund-Dudas C, Simoff M, et al. Smoking and lung cancer survival: the role of comorbidity and treatment. *Chest* 2004;125(1):27-37.

22. Kjaerbye-Thygesen A, Frederiksen K, Hogdall EV, et al. Smoking and overweight: negative prognostic factors in stage III epithelial ovarian cancer. *Cancer Epidem Biomar* 2006;15(4):798-803.
23. Browman GP, Wong G, Hodson I, et al. Influence of cigarette smoking on the efficacy of radiation therapy in head and neck cancer. *N Engl J Med* 1993;328(3):159-63.
24. Gong Z, Agalliu I, Lin DW, et al. Cigarette smoking and prostate cancer-specific mortality following diagnosis in middle-aged men. *Cancer Cause Control* 2008;19(1):25-31.
25. National Cancer Institute. Smoking in cancer care (PDQ®). Updated on 5 August 2013. Available at: <http://cancer.gov/cancertopics/pdq/supportivecare/smokingcessation/HealthProfessional>. Accessed on 22 April 2014.
26. Ramamoorthy S, Luo L, Luo E, et al. Tobacco smoking and risk of recurrence for squamous cell cancer of the anus. *Cancer Detect Prev* 2008;32(2):116-20.
27. Gillison ML, Zhang Q, Jordan R, et al. Tobacco smoking and increased risk of death and progression for patients with p16-positive and p16-negative oropharyngeal cancer. *J Clin Oncol* 2012;30(17):2102-11.
28. Alsadius D, Hedelin M, Johansson K, et al. Tobacco smoking and long-lasting symptoms from the bowel and the anal-sphincter region after radiotherapy for prostate cancer. *Radiother Oncol* 2011;101(3):495-501.
29. Balduyck B, Sardari Nia P, Cogen A, et al. The effect of smoking cessation on quality of life after lung cancer surgery. *Eur J Cardio-thoracic* 2011;40(6):1432-8.
30. Do K, Johnson MM, Lee JJ, et al. Longitudinal study of smoking patterns in relation to the development of smoking-related secondary primary tumors in patients with upper aerodigestive tract malignancies. *Cancer* 2004; 101(12):2837-42.
31. Garces Y I, Schroeder DR, Nirelli LM, et al. Second primary tumors following tobacco dependence treatments among head and neck cancer patients. *Am J Clin Oncol* 2007;30(5):531-9.
32. Do K, Johnson MM, Doherty DA, et al. Second primary tumors in patients with upper aerodigestive tract cancers: Joint effects of smoking and alcohol (United States). *Cancer Cause Control* 2003;14(2):131-8.
33. Richardson GE, Tucker MA, Venzon DJ, et al. Smoking cessation after successful treatment of small-cell lung cancer is associated with fewer smoking-related second primary cancers. *Annals Intern Med* 1993;119(5):383-90.
34. van Leeuwen FE, Klokman WJ, Stovall M, et al. Roles of radiotherapy and smoking in lung cancer following Hodgkin's disease. *J Natl Cancer Inst* 1995;87(20):1530-7.
35. Travis LB, Gospodarowicz M, Curtis RE, et al. Lung cancer following chemotherapy and radiotherapy for Hodgkin's disease. *J Natl Cancer Inst* 2002;94(3):182-92.
36. Kinoshita Y, Tsukuma H, Ajiki W, et al. The risk of second primaries in gastric cancer patients: Adjuvant therapy and habitual smoking and drinking. *J Epidemiol* 2000;10(5):300-4.

VI. Treatment Toxicity, Treatment Tolerance and Recovery

Background

Smoking during cancer treatment can increase the risk of treatment related toxicity and complications. Literature has shown that smokers have greater symptoms and toxicity on treatment. Additionally, more of these symptoms are severe.^{1,2} Late effects and delayed recovery are also more prevalent in smokers compared to those who do not smoke on treatment.² Treatments such as surgery, chemotherapy, drug treatment and radiation can all be more tolerable and more effective if smoking cessation is implemented. Smoking cessation is important at any point of the cancer journey. It is particularly important for the effectiveness and tolerance of cancer treatment. Key evidence highlighted below illustrates the negative impact of smoking with respect to chemotherapy response, radiation therapy related side effects, surgical complications and late effects of treatment.

Key Evidence

Smoking can be associated with treatment complications such as pneumonia, increased post-operative complication rates, longer hospital stays and increased hospital death in surgical patients.³⁻⁶ For example, for patients treated with breast cancer surgery, Sorensen et al. quote, “Independent of confounders and other significant risk factors, smokers have a higher risk of post–mastectomy wound infections, skin flap necrosis and epidermolysis than non-smokers”.⁷

Smoking is a negative predictor in response to chemotherapy in lung cancer patients.⁸ Continued smoking is associated with dose delays and reductions (odds ratio, 11.21; $p = 0.01$).⁹ Additionally, circulating tobacco smoke can impact the metabolism of many drugs. For example, erlotinib concentration can be as little as half of that of non-smokers.¹⁰

Radiation treatment related side effects are more significant for those who smoke. In one study, smoking was seen as one of the greatest predictors of major complications during radiation therapy.¹¹ Mucositis can last nearly twice as long for smokers compared to those who do not smoke while on treatment.¹² Increased risks of bladder and rectal complications are seen in those who continue to smoke.¹¹ Infections and esophageal complications are seen less in those who quit smoking while undergoing radiation.¹³ There is an increase in the need for hospitalization while undergoing radiation therapy treatment in those who continue to smoke.¹⁴

While the literature shows a positive relationship between time from initiation of smoking cessation to treatment start and reduction in treatment related complications, it also suggests any period of smoking cessation is beneficial. The literature states that “non-active smokers (participants who smoked at baseline but stopped smoking during treatment) had symptom burden levels similar to those of non-smokers”.¹ Additionally, through a retrospective review of surgical patients who underwent primary resections for lung cancer, Mason et al. found that smoking, in comparison to never smoking, increased the risk of hospital mortality (1.5% versus 0.39%) and risk of pulmonary complications (6.9% versus 2.6%).⁶ However, notably, an inverse relationship exists between the risk of these complications and pre-operative smoking cessation interval.⁶ Current smokers had an estimated odds ratio of 1.8 (95% CI, 1.05 to 3.1); comparatively, the estimate odds ratios for patients who quit smoking 14 days to

1 month, 1 to 12 months or > 12 months prior to surgery were 1.6 (95% CI, 0.85 to 3.1), 1.5 (95% CI, 0.81 to 2.8) and 1.3 (95% CI, 0.77 to 2.2), respectively.⁶

“In addition to decreased quality of life during and after treatment, smokers were at increased risk of treatment interruption and decreased response to radiation, given the higher rate of complications”.¹⁴ Broman and colleagues further solidified this evidence demonstrating a lower rate of complete response (45% versus 74%; $p = 0.008$) and poorer 2-year survival (39% versus 66%; $p = 0.005$) in patients who continued to smoke during radiation treatment compared to those who did not (abstainers and never smokers).¹⁵

Late effects are more pronounced in smokers compared to those who do not smoke during treatment. In fact, active smokers were found to have a significantly increased incidence of grade three or greater late complications compared to former smokers (49% versus 31%; $p=0.01$).² Most concerning is that these late treatment effects can extend over a significant period of time. Evidence shows that smokers report a higher total symptom burden than non-smokers at their six month follow-up (27.7 versus 21.9; $p<0.05$), and this pattern is known to extend even further.¹ One study assessing late effects in prostate cancer patients who received radiation treatment to the pelvis found that current smokers had a higher risk of developing *long-lasting* symptoms from the bowel and anal-sphincter region.¹⁶

Recommendation

Patients who smoke should be encouraged to stop. Stopping at any point during the cancer treatment journey is found to be beneficial. Smoking cessation can decrease treatment-related toxicity and improve tolerance. It also decreases late effects of surgery/recovery, radiation, chemotherapy and drug treatments.

References

1. Peppone LJ, Mustian KM, Morrow GR, et al. The late effect of cigarette smoking on cancer treatment-related side effects. *Oncologist* 2011;16(12):1784-92.
2. Chen J, Chen LM, Vaughan A, et al. Tobacco smoking during radiation therapy for head-and-neck cancer is associated with unfavorable outcome. *Int J Radiat Oncol Biol* 2011;79(2):414-9
3. Purkey MT, Levine MS, Prendes B, et al. Predictors of aspiration pneumonia following radiotherapy for head and neck cancer. *Annals Otol Rhinol Laryngol* 2009;118(11):811-6.
4. Erhunmwunsee L & Onaitis MW. Smoking cessation and the success of lung cancer surgery. *Curr Oncol Rep* 2009;11(4):269-74.
5. Ehlers SL, Gastineau DA, Patten CA, et al. The impact of smoking on outcomes among patients undergoing hematopoietic stem cell transplant for the treatment of acute leukemia. *Bone Marrow Transpl* 2011;46(2):285-90.
6. Mason DP, Subramanian S, Nowicki ER, et al. Impact of smoking cessation before resection of lung cancer: a society of thoracic surgeons general thoracic surgery database study. *Annals Thorac Surg* 2009;88(2):362-71.

7. Sorensen LT, Horby J, Friis E, et al. Smoking as a risk factor for wound healing and infection in breast cancer surgery. *Eur J Surg Oncol* 2002;28(8):815-20.
8. Duarte RLM, Luiz RR, Paschoal MEM. The cigarette burden (measured by the number of pack-years smoked) negatively impacts the response rate to platinum-based chemotherapy in lung cancer patients. *Lung Cancer* 2008;61(2):244-54.
9. Greer JA, Pirl WF, Park ER, et al. Behavioral and psychological predictors of chemotherapy adherence in patients with advanced non-small cell lung cancer. *J Psychosomat Res* 2008;65(6):549-52.
10. Hamilton M, Wolf JL, Rusk J, et al. Effects of smoking on the pharmacokinetics of Erlotinib. *Clin Cancer Res* 2006;12(7 pt 1):2166-71.
11. Eifel PJ, Jhingran A, Bodurka DC, et al. Correlation of smoking history and other patient characteristics with major complications of pelvic radiation therapy for cervical cancer. *J Clin Oncol* 2002;20(17):3651-7.
12. Rugg T, Saunders MI, Dische S. Smoking and mucosal reactions to radiotherapy. *Brit J Radiol* 1990;63(751):554-6.
13. Nieder C & Bremnes RM. Effects of smoking cessation on hypoxia and its potential impact on radiation treatment effects in lung cancer patients. *Strahlenther Onkol* 2008;184(11):605-9.
14. Zevallos JP, Mallen MJ, Lam CY, et al. Complications of radiotherapy in laryngopharyngeal cancer. *Cancer* 2009;115(19):4636-44.
15. Browman GP, Wong G, Hodson I, et al. Influence of cigarette smoking on the efficacy of radiation therapy in head and neck cancer. *N Engl J Med* 1993;328(3):159-63.
16. Alsadius D, Hedelin M, Johansson K, et al. Tobacco smoking and long-lasting symptoms from the bowel and the anal-sphincter region after radiotherapy for prostate cancer. *Radiother Oncol* 2011;101(3):495-501.

VII. Clinical Considerations

- All cancer patients should be asked their smoking status and have their smoking status documented in their medical chart.
- Patients achieve benefits from smoking cessation at any point in their cancer journey, and should be encouraged to quit throughout their treatment, recovery and into survivorship. Greatest benefit can be realized through cessation interventions which are provided as early as possible in the cancer journey.
- Patients and family members should be educated on the impact of smoking on their cancer treatment.
- If the patient smokes, or if they have recently quit, they should be advised to stop or stay quit, and offered access to a smoking cessation program.
- Patients who have difficulties with quitting smoking will need continued support and encouragement from the healthcare team and a smoking cessation program.
- Patients may blame themselves for their illness. It is important that healthcare providers explain the strong role of nicotine addiction and motivate their patients to quit smoking by using the social support of family, friends and healthcare professionals.

VIII. Referrals

Smoking cessation programs are offered at CancerCare Manitoba. The clinic is operated by a multidisciplinary team that includes nurses, nurse practitioners, and support from psychosocial oncology and pharmacy.

Who Is Eligible?

- Oncology patients from all over Manitoba
- Families of CancerCare Manitoba patients
- CancerCare Manitoba staff

Making a Referral

Referrals to the MacCharles CancerCare Manitoba Quit Smoking Clinic can be made by:

- Calling the self-referral hotline at 204-787-1202 or toll-free 1-888-775-9899
- Contacting the Referrals office by fax at 204-786-0621

Once a referral is received, it is triaged by a clinic nurse and delegated to nursing and/or psychosocial staff. A member of our team will then contact the patient to discuss the program and set up an appointment.

For those outside of Winnipeg, telehealth or teleconference services can be used to access support offered through the Quit Smoking Clinic at CancerCare Manitoba.

IX. Implementation and Dissemination

The value of guidelines truly lies in their implementation and use. For that purpose, consideration was given to implementation during the planning and drafting of this guideline document.

CancerCare Resources

It was recognized that resources would be needed to distribute these guidelines to the community. For that purpose, the guideline will be accessible online through the CancerCare Manitoba website. Online availability will be preceded by an e-blast notification with the website embedded. Announcement of the guideline and updates will be through established provincial communication Smoking Channels; Community Oncology Program to CCPN rural sites, UPCON clinics and WRHA Community Oncology Program sites. This guideline will also be provided to partner organizations and guideline reviewers in other provinces. Use of the guideline in clinics will be through the online version.

Educational Events

Presentation of the guideline's recommendations will be made available at rounds and conferences; for example DSG conference rounds, CCMB Hematology/Oncology Regional Grand rounds, Allied Health rounds (Patient Services rounds), Community Cancer Care Educational Conference and at UPCON education and training events. In addition, presentations will be made at CCMB's Cancer Hubs as part of the Manitoba Tobacco Reduction Alliance (MANTRA) initiative.

Smoking Cessation in Practice

The evidence presented in this guideline substantiates the importance of smoking cessation initiatives at CancerCare Manitoba. For this purpose, smoking, as a vital sign, has been incorporated into the Comprehensive Problem and Symptom Screening (COMPASS) tool utilized at CCMB. The COMPASS tool allows practitioners to identify patients who are smoking and provides an opportunity for practitioners to inform patients about the impact of smoking on their cancer diagnosis and refer them to the Quit Smoking Program (*See Section VIII - Referrals*).

X. Contact Practitioner and Contributors

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XI. Conflict of Interest

In accordance with the CCMB policy no. 01.001, “Conflict of Interest”, the authors of this guideline declare that no commercial support was received during the development of this guideline. No relationships with commercial interests exist.

XII. Appendix

Levels of Evidence

| | |
|------------|---|
| Ia | Evidence obtained from meta-analysis of randomised controlled trials |
| Ib | Evidence obtained from at least one randomised controlled trial |
| IIa | Evidence obtained from at least one well-designed controlled study without randomisation |
| IIb | Evidence obtained from at least one other type of well-designed, quasi- experimental study |
| III | Evidence obtained from well-designed, non-experimental descriptive studies, such as comparative studies, correlation studies and case studies |
| IV | Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities |

British Committee for Standards in Haematology 2007 <http://www.bcsghguidelines.com>

XIII. Patient Resources

- Smoking Cessation: A Quit Smoking Guide for Cancer Patients, CancerCare Manitoba. Handbook.
- Guide to Quitting Smoking, American Cancer Society. Available at:
<http://www.cancer.org/acs/groups/cid/documents/webcontent/002971-pdf.pdf>

CancerCare Manitoba
675 McDermot Avenue
Winnipeg, Manitoba, Canada
R3E 0V9
www.cancercare.mb.ca
CCMB Clinical Practice Guideline: **Supportive Care**
Smoking Cessation in Oncology
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