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Clinical Practice Guidelines - Thoracic Disease Site

Guideline Title:	Surveillance and Follow-up of Patients after Curative Intent Treatment for Non-Small Cell Lung Cancer	**Date:**	**(O):** **(R):**	Nov 30, 2018
Tumor Group:	Thoracic Disease Site Group	**Page:**		1 of 9
Issuing Authority:	Dr. Jehan Siddiqui Clinical Chief, Cancer Care Program	**Date Signed:**		Feb 19, 2019
Adapted From:	Cancer Care Ontario's "Follow-up and Surveillance of Curatively Treated Lung Cancer Patients" guideline, August 2014 (39).			

Introduction:

Historically, the value of a follow-up and surveillance plan for patients treated for non-small cell lung cancer (NSCLC) was uncertain. Distant metastasis accounted for the majority of recurrences with no chance for cure. Computed tomography (CT) has been shown to have an advantage over chest x-ray of improved early detection of intrathoracic locoregional recurrences and new metachronous thoracic lesions, which may be amenable for curative intent treatment (1). In addition, the advent of new chemotherapy treatment options which may improve survival for those with recurrent lung cancer also have created an important focus shift toward long-term follow-up survivorship care. Evidence is also growing to support the transition of safe and effective follow-up care from the specialty cancer center to that of the primary care or family physician (2-4). Nevertheless, no national or international consensus exists on the optimal clinical follow-up and surveillance strategy for patients who received curative intent treatment for NSCLC. Currently in Newfoundland and Labrador, there are no provincial guidelines for physicians (i.e. family physicians, surgeons, oncologists) and nurse practitioners to follow to coordinate the follow-up care and imaging required for this patient cohort. The Eastern Health Thoracic Disease Site Group has decided to adapt Cancer Care Ontario's (CCO) interpretation of an optimal strategy for clinical follow-up and imaging surveillance for this cohort (39). The CCO guideline is evidence-based and consensus-formed by a panel of Canadian lung cancer experts.

Questions:

What is the optimal clinical follow-up and imaging surveillance for patients with stage I – III NSCLC post-treatment?

Target Population:

These recommendations apply to all patients with stage I – III NSCLC, who have received treatment with curative intent and require follow-up and imaging surveillance for the purpose of disease control.

Supporting Evidence:

Patients who have undergone surgical treatment for lung cancer are deemed at high risk for recurrence of the initial cancer (10% - 38% overall risk) or the development of a new separate or metachronous primary lung tumor (1% – 2% per year risk) (5,6). The pattern of recurrent lung cancer occurs either as locoregional intrathoracic disease, distant metastases, or both. The majority of recurrences are found to be distant metastases, with the majority commonly found in the brain, bones, liver, and adrenals, which are considered to be incurable and therefore treated with palliative intent. The detection of intrathoracic locoregional recurrent disease rates have been reported to be 15% to 39%, dependent upon the stage of initial cancer (7-9). The more common sites of locoregional intrathoracic recurrence include parenchymal lesions, hilar lymphadenopathy, pleural nodules or effusions, and lesions on the ribs or at the surgical incision site. A study at Memorial Sloan-Kettering Cancer Center in New York found survival outcomes of patients treated for NSCLC to be significantly worse for patients with recurrences (24%) compared to those with a new second primary tumor (67%) ($P < .001$) (8). However, this study also found that in select cases the use of second-line local therapy in the form of surgery, radiation therapy, or both may be offered with potentially curative intent for 25% to 30% of isolated locoregional recurrences. Several studies have found that most recurrences occur within the first two years post-treatment however, the risk remains high up to five years post-treatment (8-11). Hence, most national and international guidelines favor more frequent imaging during the first two years which taper off to annually at around year five (30,32-37).

The elevated risk for the development of a second new primary lung cancer also encourages the use of imaging surveillance for detecting new lesions early, making them amenable to treatment and increasing the potential for cure. The criteria used to establish a metachronous tumor include whether it has a different histologic type from the first primary lung cancer, or the same histologic type with a disease-free interval of at least 2 years; the tumor originated from carcinoma in situ; or its' location in a different lobe or lung, with no carcinoma in the lymphatic vessels which are common to both, no extra-pulmonary metastases at the time of diagnosis, and a different DNA ploidy (7).

The CCO evidence-based guideline entitled "Follow-up and Surveillance of Curatively Treated Lung Cancer Patients" recommends a follow-up and surveillance plan which the Eastern Health Thoracic Disease Site Group supports for all lung cancer survivors treated with curative-intent (39). The CCO guideline outlines that all patients diagnosed and treated for stages I - III NSCLC should undergo clinical evaluation which includes a medical history and physical examination every three months in years one and two, every six months in year three, and annually thereafter. Chest imaging with CT should be performed post-treatment at three months, six months, and then every six months until end of year two, and then annually until year five. It will be at the discretion of the healthcare professional whether to continue annual imaging after year five, dependent upon whether the patient's health status would tolerate further treatment if a new cancer or recurrence is detected.

The growing global trend of transitioning the follow-up care of oncology patients after curative-intent treatment to their primary care physicians is being carried out all across Canada. Choosing Wisely Canada, a Canadian healthcare initiative, has offered ten recommendations which physicians can advocate to promote the sustainability of the health care system (12). One of these recommendations is that effective follow-up care can, and should be, offered in settings where financial costs are lower (i.e., primary care) rather than those where the financial costs are much higher (i.e., tertiary care). This proposal reduces the strain on tertiary care settings, such as outpatient cancer centers, which in turn allows for the limited resources to be used on the care of patients who are newly diagnosed, those patients receiving active treatment, and the follow-up of more complex cases (13). Therefore, the surveillance and follow-up of patients treated with curative intent may be provided by specialists, family physicians, or nurse practitioners. Therefore, after their completion of the treatment regimen, the patient may be discharged from the Dr. H. Bliss Murphy Cancer Center to the care of the primary healthcare provider as identified by the patient. A discharge letter will be forwarded to the healthcare provider, as well as provided to the patient outlining the follow-up and surveillance schedule recommended by the Eastern Health Thoracic Disease Site Group.

Clinical examination is a crucial component of the follow-up strategy. It allows the recognition and potential alleviation of post-treatment effects; detection and treatment of new symptomatology indicative of recurrent disease or a new primary cancer; and counselling on wellness and health-related quality of life (QoL). A 2011 American Cancer Society study on cancer survivors found that lung cancer survivors experience a high symptom burden on health-related QoL one year after their diagnosis and treatment (14). Moreover, a study which looked at the effects on QoL following surgical resection of NSCLC found a sustained decrease in multiple QoL domains for these patients (15). Several prospective cohort studies of lung cancer survivors have also identified many non-recurrence related issues, such as dyspnea, cough, fatigue, impaired breathing, pain, reduced sleep quality, and decline in appetite (16-19). Investigation of symptoms suggestive of a recurrence or a new lung primary is also another important objective of the clinical examination. A recent systematic review and meta-analysis assessed the survival benefits of conducting follow-up on lung cancer patients after curative-intent therapy (20). It found that symptomatic patients who were diagnosed with recurrent disease fared worse than those with asymptomatic recurrences, and therefore requiring the intervention of palliative care services sooner. Hence, the evaluation of the patient for new or worsening symptomology indicative of recurrence, such as respiratory symptoms or neurological symptoms, is fundamentally important during follow-up clinical examination (32).

The systematic review and meta-analysis described earlier also revealed that detecting asymptomatic recurrences early has been associated with a trend for longer survival (20). There is also some evidence to suggest that the majority of recurrences are detected within the first two years after treatment with curative-intent (21). Hence, the role of imaging surveillance with higher frequency in the initial two years and decreasing to annually at five years and beyond is a prudent recommendation.

There are presently no randomized clinical trial data to indicate whether chest CT imaging is superior to chest radiography in the surveillance and follow-up of curatively-treated NSCLC patients. However, several influential and respected oncology organizations have recently published recommendations for the use of chest CT as the optimal imaging modality for surveillance screening for this cohort. These include the American Association for Thoracic

Surgery (AATS), American College of Chest Physicians (ACCP), Cancer Care Ontario (CCO), European Society for Medical Oncology (ESMO), National Comprehensive Cancer Network (NCCN), and Up-To-Date (UTD) guideline organization (35,37,39-43). Some of these organizations have based their recommendations on retrospective data while others have cited data from the recent American National Lung Screening trials, which have found that low-dose chest CT scans were more sensitive than CXR for the detection of early-stage lung cancers (22,23). It has also been suggested that the use of low-dose CT can achieve a reduction in mortality from lung cancer in experienced U.S. screening centers. Likewise, a recent prospective Canadian study looked at 291 patients who had received complete surgical resection of their lung cancer which found that minimal-dose CT was superior to CXR for the detection of both new and recurrent lung cancer (24). Furthermore, the new or recurrent cancers detected by minimal-dose CT were more likely to be detected at an earlier stage while the patient was still asymptomatic and treated with curative-intent resulting in longer survival than those treated with palliative-intent (69 months vs 25 months; $P < .0001$). The rationale behind the use of low-dose or minimal-dose CT, as opposed to standard-dose CT, is to reduce the dose of radiation exposure to the at-risk population. The radiology departments throughout the province of NL are presently providing relatively low-dose CT scanning as a standard for our population and therefore, the Eastern Health Thoracic Disease Site Group has decided to forgo using language regarding CT dosing to prevent confusion among physicians.

Little and conflicting trial data exist to show any statistically significant role for positron emission tomography (PET-CT) in the routine surveillance and detection of new or recurrent lung cancer. Moreover, none of the prominent oncology guideline development organizations such as CCO, NCCN, and UTD recommend its utility in this circumstance (39-43). Therefore at present, PET-CT is not currently recommended in the routine imaging surveillance of curatively treated lung cancer patients. PET-CT can still play a role in determining the extent of suspected metastatic spread or assisting in the evaluation of new abnormalities detected on CT.

Important contributions have also been identified in the maintenance of the health and well-being of lung cancer survivors. The 2018 NCCN guideline have included recommendations for the long-term follow-up care strategy for NSCLC cancer patients (41). These include up-to-date immunizations, smoking cessation, maintaining a healthy weight, being physically active, consuming a healthy diet, and limiting alcohol consumption. The Eastern Health Thoracic Disease Site Group agrees with this strategy, and recommends that all patients who have received curative-intent therapy for lung cancer should be considered for an annual influenza vaccination and an up-to-date pneumococcal vaccination (or revaccination) as needed. Though this recommendation is important for the majority of these patients, it is especially pertinent for those with chronic pulmonary disease, such as COPD, asthma, as well as smokers, who are more at risk from influenza viruses and pneumococcal disease in terms of morbidity and mortality (25-27). This particular population account for a large proportion of patients who present in the clinical setting with a diagnosis of lung cancer. In addition, organizations such as the American Cancer Society and the Public Health Agency of Canada recommend these vaccinations for oncology patients even while receiving chemotherapy, as long as the vaccination does not contain live virus (28-31). The Eastern Health Thoracic Disease Site Group also recommends a herpes zoster vaccination though its use is optional due to a live virus content which will require a joint family physician-patient decision on the appropriateness of use.

Two Cochrane Reviews have reported benefit in smoking cessation counselling, in the form of both behavioral and pharmacotherapy support, as well as health care professional advice (32,33). Therefore, the Eastern Health Thoracic Disease Site Group suggests that all health care professionals encourage their patients who smoke to take advantage of the available resources for smoking cessation.

The follow-up and surveillance program for patients after curative-intent treatment of NSCLC will be coordinated by a designated physician, or nurse practitioner, as per the written request of the oncology specialist at the Dr. H. Bliss Murphy Cancer Center. The use of appropriate clinical exam and imaging modalities will aid in eliminating the redundancy and overuse of imaging resources by multiple sources, as well as, reducing patient stress and anxiety brought on by unnecessary multiple testing.

Recommendations:

The following recommendations of the Eastern Health Thoracic Disease Site Group apply to patients diagnosed with stage I – III NSCLC, who have completed curative intent treatment, are asymptomatic, have no physical findings or laboratory abnormalities to suggest metastatic disease, and require routine follow-up and surveillance:

- Following curative-intent treatment, patients should receive scheduled follow-up visits that include a medical history and physical examination every 3 months in years one and two, every 6 months in year three, and annually thereafter;
- In addition, these patients should also undergo chest CT imaging post-treatment at 3 months, 6 months, and then every 6 months until the end of year two, then annually until end of year five.
  Note: Health care professionals should use their own discretion whether to continue yearly imaging after year five, dependent upon the patient's performance status and ability to undergo treatment if a new or recurrent cancer is detected;
- PET-CT is not recommended in the routine surveillance of curatively treated lung cancer;
- Patients with an history of NSCLC who have been treated with curative-intent therapy require surveillance which may be provided by specialists, family physicians, or nurse practitioners;
- Any new, persistent or worsening symptom warrants the consideration of a recurrence, especially:
  - Constitutional symptoms (new or unexplained) such as dysphagia, fatigue, nausea and vomiting, finger clubbing, lymphadenopathy, sweats, thrombosis, weight loss, or loss of appetite,
  - Pain such as bone pain, chest pain, or caveat shoulder pain unrelated to trauma,
  - Neurological symptoms such as persistent headaches or new neurological signs suggestive of brain metastases or cord compression such as leg weakness, speech changes, headache or focal neurological symptoms,
  - Respiratory symptoms such as cough, dyspnea, hemoptysis, hoarseness, signs of superior vena cava obstruction, or stridor;
- Health-related quality of life (QoL) is very important for long-term survivors suffering from late side effects of their curative-intent therapy (including surgery, radiation therapy and chemotherapy). Issues and long-term effects experienced by NSCLC survivors should be addressed by health care professionals to aid in coping with these symptoms to improve QoL:

  - Constitutional issues, such as anxiety, depression, cough, shortness of breath, fatigue, pain, sleep disturbances, dysphagia, esophageal stricture, limitations in physical activity, and general health deterioration,
  - Long-term chemotherapy effects, such as hearing loss, neuropathies, and renal impairment,
  - Long-term radiation therapy effects, such as breathing complications, breathlessness, or dyspnea,
  - Long-term surgery effects, such as oxygen dependence, post-thoracotomy pain syndrome, reduce exercise tolerance or activity limitations, shortness of breath;
- All lung cancer survivors should be encouraged to maintain a healthy weight, to be physically active, to consume a healthy diet, and limit their alcohol consumption;
- All lung cancer survivors should be considered for an annual influenza vaccination, as well as, a pneumococcal vaccination as needed. An up-to-date herpes zoster vaccine is optional based upon the discretion of a joint family physician-patient decision;
- Smoking cessation counselling, in the form of behavioral and pharmacotherapy support, as well as health care professional advice is recommended for all patients, who received curative-intent treatment for NSCLC.

Note: These guidelines do not apply to patients with a confirmed tumor recurrence, or stage IV disease.

Search Strategy:

Literature searches were conducted in PubMed, Embase, and the Cochrane Library, using keywords “lung neoplasms” AND “surveillance” AND “follow-up”, as well as a manual search of the reference lists of available literature articles. All selected literature articles and source guidelines were in English and dated after December 1, 2012 (unless the selection was an earlier landmark study) up to November 3, 2018. Guideline searches were also carried out on the websites of the world’s most highly respected cancer organizations and agencies. The inclusion/exclusion process consisted of selecting guidelines from reputable cancer organizations with preference given to those from Canadian sources where possible. Ten source guidelines were identified and conformed to our search criteria, from which six were selected due to currency, quality of content and/or were Canadian in origin (34-43).

The six identified source guidelines (35, 37- 43) were put through the ADAPTE process (44) with an AGREE II assessment (45), and the Cancer Care Ontario (CCO) ‘Follow-up and Surveillance of Curatively Treated Lung Cancer Patients” guideline was chosen to be adapted for use in our guideline (39). The CCO guideline was selected as the optimal choice due to its applicability and currency of content.

There has been much debate but no consensus on the ‘grading of evidence’ in Canada. Presently, Canadian experts in the field of guideline development are involved in an ongoing in-depth analysis of the functionality of grading. Until such time as a report is released of their findings, and a consensus reached on whether to assign a grade of recommendation to a guideline, this group has decided to forgo the use of grading.

No competing or conflicts of interest were declared by membership of the Lung Disease Site Group.

Disclaimer:

These guidelines are a statement of consensus of the Thoracic Disease Site Group regarding their views of currently accepted approaches to diagnosis, treatment and follow-up. Any clinician seeking to apply or consult the guidelines is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment.

Contact Information:

For more information on this guideline, please contact Dr. Jonathan Greenland MD FRCPC, Dr. H. Bliss Murphy Cancer Center, St. John's, NL; Telephone 709-777-2440. For access to any of our guidelines, please visit our Cancer Care Program website at www.easternhealth.ca

Literature Support:

1. Hanna WC & Keshavjee S. How to follow up patients after curative resection of lung cancer. *Semin Thoracic Surg*. 2013;25(3):213-217.
2. Lupichuk S, Nixon NA, et al. Transition of breast cancer survivors to primary care: A population-based evaluation of practice in Alberta. *Oncol Exchange.* 2016;15(4):12-17.
3. Del Giudice ME, Grunfield E, et al. Primary care physicians' views of routine follow-up care of cancer survivors. *J Clin Oncol.* 2009;27(20):3338-3345.
4. Grunfield E, Levine MN, et al. Randomized trial of long-term follow-up for early-stage breast cancer: A comparison of family physician versus specialist care. *J Clin Oncol.* 2006;24(6):848-855.
5. Haraguchi S, Koizumi K, et al. Surgical treatment of metachronous nonsmall cell lung cancer. *Ann Thorac Cardiovasc Surg*. 2010;16(5):319-325.
6. Pepek JM, Chino JP, et al. How well does the new lung cancer staging system predict for local/regional recurrence after surgery? A comparison of the TNM 6 and 7 systems. *J Thorac Oncol.* 2011;6(4):757-761.
7. Mollberg NM & Ferguson MK. Postoperative surveillance for non-small cell lung cancer resected with curative intent: Developing a patient-centered approach. *Ann Thorac Surg*. 2013;95:1112-1121.
8. Lou F, Huang J, et al. Patterns of recurrence and second primary lung cancer in early-stage lung cancer survivors followed with routine computed tomography surveillance. *J Thorac Cardiovasc Surg*. 2013;145(1):75-82.
9. Endo C, Sakurada A, et al. Results of long-term follow-up of patients with completely resected non-small cell lung cancer. *Ann Thorac Surg*. 2012;93(4):1061-1069.
10. Hung JJ, Hsu WH, et al. Post-recurrence survival in completely resected stage I non-small cell lung cancer with local recurrence. *Thorax*. 64:192-196.
11. Backhus LM, Farjah F, et al. Imaging surveillance and survival for surgically resected non-small cell lung cancer. *J Surg Res*. 2016;200:171-176.
12. Choosing Wisely Canada. Choosing wisely in oncology: Ten things physicians and patients should question. www.choosingwiselycanada.org
13. Maroun J & Alsaffar H. Evolving strategies in followup for cancer patients: A collaborative model provides a bridge between tertiary and primary care. *Oncol Exchange.* 2016;15(4):18-20.
14. Shi Q, Smith TG, et al. Symptom burden in cancer survivors 1 year after diagnosis. *Cancer*. 2011;117:2779-2790.

15. Ilonen IK, Rasanen JV, et al. Quality of life following lobectomy or bilobectomy for non-small cell lung cancer, a two-year prospective follow-up study. *Lung Cancer.* 2010;70(3):347-351.
16. Cheville AL, Novotny PJ, et al. Fatigue, dyspnea, and cough comprise a persistent symptom cluster up to five years after diagnosis with lung cancer. *J Pain Symptom Manage.* 2011;42(2):202-212.
17. Gooneratne NS, Dean GE, et al. Sleep and quality of life in long-term lung cancer survivors. *Lung Cancer.* 2007;58(3):403-410.
18. Yang P, Cheville AL, et al. Quality of life and symptom burden among long-term lung cancer survivors. *J Thorac Oncol.* 2012;7(1):64-70.
19. Tishelman C, Degner LF, et al. Symptoms in patients with lung carcinoma: Distinguishing distress from intensity. *Cancer.* 2005;104(9):2013-2021.
20. Calman L, Beaver K, et al. Survival benefits from follow-up of patients with lung cancer: A systematic review and meta-analysis. *J Thorac Oncol*. 2011;6(12):1993-2004.
21. Sugimura H, & Yang P. Long-term survivorship in lung cancer: A review. *Chest*. 2006;129(4):1088-1097.
22. The National Lung Screening Trial Research Team. Results of initial low-dose computed tomographic screening for lung cancer. *N Engl J Med.* 2013;368(21):1980-1991.
23. Aberle DR, DeMello S, et al. Results of the two incidence screenings in the National Lung Screening Trial. *N Engl J Med.* 2013;369(10):920-931.
24. Hanna WC, Paul NS, et al. Minimal-dose computed tomography is superior to chest x-ray for the follow-up and treatment of patients with resected lung cancer. *J Thorac Cardiovas Surg.* 2014;147(1):30-35.
25. Torres A, Blasi F, et al. Which individuals are at increased risk of pneumococcal disease and why? Impact of COPD, asthma, smoking, diabetes, and/or chronic heart disease on community-acquired pneumonia and invasive pneumococcal disease. *Thorax.* 2015;70:984-989.
26. Mirsaeidi M, Ebrahimi G, et al. Pneumococcal vaccine and patients with pulmonary diseases. *Am J Med.* 2014;127(9):886.e1 – 886.e8.
27. Sehatzadeh S. Influenza and pneumococcal vaccinations for patients with chronic obstructive pulmonary disease (COPD): An evidence-based analysis. *Ont Health Technol Assess Ser* [internet]. 2012 Mar;12(3):1-64. Retrieved from: www.hqontario.ca/en/mas/tech/pdfs/2012/rev_COPD_Vaccinations_March.pdf.
28. American Cancer Society. Treatment and support: Vaccination during cancer treatment. Last revised Feb 2017. Retrieved from: www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/infections/vaccination-during-cancer-treatment.html
29. Public Health Agency of Canada. Vaccine uptake in Canadian adults: Results from the 2014 adult National Immunization Coverage Survey. 2016. Retrieved from: www.canada.ca/en/public-health/services/publications/healthy-living/vaccine-uptake-canadian-adults-results-2014-adult-national-immunization-coverage-survey.html
30. Nordoy T, Aaberge IS, et al. Cancer patients undergoing chemotherapy show adequate serological response to vaccinations against influenza virus and *Streptococcus pneumoniae. Med Oncol.* 2002;19(2):71-78.
31. Tsang V. Vaccination recommendations for the hematology and oncology and post-stem cell transplant populations. *Adv Pract.* 2012;3(2):71-83.
32. Stead LF, Buitrago D, et al. Physician advice for smoking cessation. *Cochrane Database of Systematic Reviews.* 2013;5:CD000165.
33. Stead LF, Koilpillai P, et al. Combined pharmacotherapy and behavioural interventions for smoking cessation. *Cochrane Database of Systematic Reviews.* 2016;3:CD008286.

34. Saskatchewan Cancer Agency. Follow-up guidelines: Non-small cell lung cancer. September 2011. www.saskcancer.ca
35. Jaklitsch MT, Jacobson FL, et al. The American Association for Thoracic Surgery guidelines for lung cancer screening using low-dose computed tomography scans for lung cancer survivors and other high-risk groups. *J Thorac Cardiovasc Surg.* 2012;144(1):33-38.
36. British Columbia Cancer Agency. Lung: Follow-up practice guidelines. July 2012. www.bccancer.bc.ca/health-professionals/professional-resources/cancer-management-guidelines/lung/lung
37. Colt HG, Murgu SD, et al. Follow-up and surveillance of the patient with lung cancer after curative-intent therapy: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest.* 2013;143(5)(suppl):e437S-e454S.
38. Alberta Health Services. Non-small cell lung cancer: Stage I – July 2014; Stage II – July 2014; Stage III – April 2012. www.albertahealthservices.ca
39. Ung YC, Souter LH, et al. Follow-up and surveillance of curatively treated lung cancer patients. August 2014. www.cancercare.on.ca
40. Postmus PE, Kerr KM, et al. Early and locally advanced non-small-cell lung cancer (NSCLC): ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2017;28 (Suppl. 4): iv1-iv21.
41. Ettinger DS, Wood DE, et al. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer (version 2.2019). November 2018. www.nccn.org
42. West HJ, Vallieres E, et al. Management of stage I and stage II non-small cell lung cancer. October 2018. www.uptodate.com
43. Schild SE, Ramalingam SS, et al. Management of stage III non-small cell lung cancer. October 2018. www.uptodate.com
44. Brouwers M, Browman G, et al. Guideline adaptation: Enhancing efficiency in guideline development and utilization. www.adapte.org
45. Brouwers M, Kho ME, et al for the AGREE Next Steps Consortium. AGREE II: Advancing guideline development, reporting and evaluation in healthcare. Can Med J. 2010.doi : 10.1503/cmaj.090449