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REVIEW ARTICLE

Follow-up care for survivors of lymphoma who have received curative-intent treatment

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ABSTRACT

Objective This evidence summary set out to assess the available evidence about the follow-up of asymptomatic survivors of lymphoma who have received curative-intent treatment.

Methods The MEDLINE and EMBASE databases and the Cochrane Database of Systematic Reviews were searched for evidence published between 2000 and August 2015 relating to lymphoma survivorship follow-up. The evidence summary was developed by a Working Group at the request of the Cancer Care Ontario Survivorship and Cancer Imaging programs because of the absence of evidence-based practice documents in Ontario for the follow-up and surveillance of asymptomatic patients with lymphoma in complete remission.

Results Eleven retrospective studies met the inclusion criteria. The proportion of relapses initially detected by clinical manifestations ranged from 13% to 78%; for relapses initially detected by imaging, the proportion ranged from 8% to 46%. Median time for relapse detection ranged from 8.6 to 19 months for patients initially suspected because of imaging and from 8.6 to 33 months for those initially suspected because of clinical manifestations. Only one study reported significantly earlier relapse detection for patients initially suspected because of clinical manifestations (mean: 4.5 months vs. 6.0 months, $p = 0.042$). No benefit in terms of overall survival was observed for patients depending on whether their relapse was initially detected because of clinical manifestations or surveillance imaging.

Summary Findings in the present study support the importance of improving awareness on the part of survivors and clinicians about the symptoms that might be associated with recurrence. The evidence does not support routine imaging for improving outcomes in this patient population.

Key Words Lymphoma, Hodgkin lymphoma, non-Hodgkin lymphoma, follow-up, relapse

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BACKGROUND

The lymphomas constitute a large group of neoplasms arising from the lymphatic system. In 2014, the Leukemia and Lymphoma Society of Canada estimated that 9000 new cases of lymphoma would be diagnosed in Canada [1000 Hodgkin lymphomas and 8000 non-Hodgkin lymphomas (NHLs)], making lymphoma the 6th most common malignancy in the country[1]. There are many types and subtypes of NHL. Worldwide, diffuse large B-cell lymphoma (DLBCL) represents the most common subtype, accounting for 30%–40% of all newly diagnosed cases[2].

Diffuse large B-cell lymphoma and Hodgkin lymphoma are considered curable with therapies that include chemotherapy, immunotherapy, and radiation; however, a significant proportion of patients will relapse, typically within the first 2 years after primary treatment. Many patients with relapse can be treated successfully for cure with salvage chemotherapy and stem-cell transplantation. For that reason, surveillance is considered important in this group to detect relapse as early as possible; the assumption is that earlier detection will lead to better outcomes by detecting subclinical disease with a lower tumour burden.

Surveillance to detect recurrence—which includes physical examination, blood tests, and imaging—is currently used to follow patients with DLBCL and Hodgkin lymphoma who are considered to be in remission after treatment. Surveillance practice, especially the frequency

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of imaging, is known to vary widely, and recent population studies have suggested that, in asymptomatic patients, significant over-testing can occur, without resulting in improved outcomes. Currently, no Canadian guidelines have summarized the evidence about the type and timing of surveillance testing for asymptomatic patients with DLBCL and Hodgkin lymphoma who have been treated for cure.

The intent of the present evidence summary was to assess the available evidence about the follow-up of asymptomatic survivors of lymphoma who have received curative-intent treatment. To direct the search for available evidence, 3 research questions were developed:

- Which clinical activities have been shown to be effective in detecting clinical recurrence or further hematologic neoplasms?
- What are the appropriate frequencies and timings for the clinical activities that have been shown to be effective in detecting clinical recurrence, further hematologic neoplasms, or malignancy?
- Which surveillance procedures have been shown to be effective in detecting therapy-related secondary malignancies after treatment for lymphoma?

METHODS

This evidence summary was developed at the request of the Cancer Care Ontario Survivorship and Cancer Imaging programs because of an absence of evidence-based practice documents in Ontario for the follow-up and surveillance of asymptomatic patients with lymphoma treated with curative intent. A Working Group consisting of 1 radiation oncologist, 2 hematologists, 1 regional primary care lead, 2 radiologists, 1 registered nurse, 2 patient representatives, and 1 health research methodologist from the Clinical Programs and Quality Initiatives was responsible for searching the literature, reviewing the identified evidence, and drafting the summary.

Literature Search Strategy

This literature search was conducted in two planned stages: a search for systematic reviews, and then a search for primary literature. Identified systematic reviews were to be assessed for quality using the AMSTAR tool[3] to determine whether the review could be incorporated into the present evidentiary base. Assuming that no systematic reviews were identified, a systematic review of the primary literature was also planned. If a suitable systematic review were to be found, a systematic review of the primary literature would be conducted starting from the date of the reported systematic review, with the goal of updating the evidence from the existing publication.

The Cochrane Database of Systematic Reviews, MEDLINE (Ovid), and EMBASE (Ovid) for January 2000 to August 2015 were searched using the term "lymphoma." Systematic reviews more than 5 years old were considered not relevant, because the main goal of the search for systematic reviews was to identify recent secondary sources covering the primary relevant literature about the follow-up care for survivors of lymphoma who had received curative-intent treatment.

In August 2015, the MEDLINE (Ovid) and EMBASE (Ovid) databases were searched for primary literature; that search was updated in March 2016. The search strategy included the MeSH term "exp lymphoma," combined with additional terms and text words for the intervention (follow-up) and the population (survivors). The results were limited to English language articles and articles published from 2000 to 2015. Table I presents the full search strategy used to retrieve potentially relevant studies.

Relevant articles were reviewed by 2 Working Group members (JS, NPV), and the reference lists of those articles were searched for additional trials. A data audit procedure conducted by an independent individual verified the accuracy of the information obtained from the studies included in this report.

Data extraction was conducted by 1 Working Group member (NPV). All extracted data and information was assessed by a second reviewer (JS) and audited by an independent individual to verify the accuracy of the information obtained from the included studies. For primary studies, key characteristics—author, year of publication, study design, study population, sample size, post-treatment follow-up protocol, and median follow-up time—were recorded. Outcomes of interest, including relapse rate, time to relapse, method of relapse detection and detection rate by follow-up activity, overall survival rate, and relapse-free survival rate, were extracted when available.

Randomized clinical trials were to be assessed for quality by examining method of randomization, reporting of blinding, power and sample size calculation, length of follow-up, reporting of details of the statistical analysis, reporting of withdrawals from treatment and other losses to follow-up, and reporting of the sources of funding for the research. Comparative, nonrandomized, and single-arm evidence was to be assessed according to full reporting of the patient selection criteria, the follow-up received by each patient, all relevant outcomes, and the source of funding.

All authors of the present report reviewed and discussed a draft, with the aim of assessing the quality of the evidence as a whole, without the use of a scoring system or cut-offs, according to the policy of the Program in Evidence-Based Care.

RESULTS

Literature Search

Of 1950 titles and abstracts identified in the search of the MEDLINE and EMBASE databases, 1841 appeared potentially eligible on initial review, and 124 of the latter were verified to be eligible for full-text review. Of the eligible publications, eleven nonrandomized retrospective full-report studies addressed follow-up care for adult or adolescent survivors of lymphoma (or both) who had received curative-intent treatment and reported the outcome of interest (overall survival) and relapse-related outcomes (relapse detected by varying follow-up schedules, such as symptomatic versus asymptomatic relapses; relapse-free survival; median time to relapse; number of imaging tests per relapse detected). The included studies involved patients with DLBCL, lymphoid malignancies, and aggressive Hodgkin lymphoma. Table II sets out the study and patient characteristics.

TABLE I Literature search strategy

Step	Ovid MEDLINE databases[a]	EMBASE
1	exp Lymphoma/(152067)	exp lymphoma/(156567)
2	(malignan$ adj5 lymphoma$).tw.(18875)	(malignan$ adj5 lymphoma$).tw.(12734)
3	1 or 2(156723)	or/1–2(158354)
4	second* primary tumo?*r**.mp.(1100)	second* primary tumo?*r**.mp.(1076)
5	(detect* adj2 relapse*).ti,ab.(985)	(detect* adj2 relapse*).ti,ab.(1327)
6	(early adj2 detect*).ti,ab.(57377)	(early adj2 detect*).ti,ab.(62554)
7	exp Neoplasms, Radiation-Induced/(17848)	exp radiation induced neoplasm/ or exp disease free survival/ or exp recurrence free survival/ or exp lymph node metastasis/ or exp tumor recurrence/ or exp tumor regression/ or exp minimal residual disease/ or exp second cancer/(189706)
8	exp disease-free survival/(49447)	follow-up.ti.(70226)
9	recurrence-free survival.mp.(6348)	surveillance.ti.(29572)
10	exp lymphatic metastasis/ or exp neoplasm recurrence, local/ or exp neoplasm regression, spontaneous/ or exp neoplasm, residual/(162901)	aftercare.ti.(547)
11	follow-up.ti.(76832)	evaluation.mp. and follow-up.ti. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword](9788)
12	surveillance.ti.(30124)	long term care.ti.(5744)
13	aftercare.ti.(688)	survivors.ti.(16502)
14	evaluation.mp. and follow-up.ti. (mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier)(9360)	or/4–13(367701)
15	long term care.ti.(7935)	exp clinical chemistry/ or exp blood examination/(160148)
16	exp Neoplasms, Second Primary/(11094)	diagnostic imaging/ or exp computer assisted tomography/(646633)
17	survivors.ab,ti.(61837)	or/15–16(794270)
18	or/4–17(449523)	3 and 14 and 17(1772)
19	exp clinical chemistry tests/ or exp hematologic tests/(352956)	(comment or letter or editorial or note or erratum or short survey or news or newspaper article or patient education handout or case report or historical article).pt.(1890233)
20	diagnostic imaging/ or exp tomography, x-ray computed/ or tomography/(366060)	18 not 19(1637)
21	or/19–20(716528)	limit 20 to english(1506)
22	3 and 18 and 21(1046)	animals/(735436)
23	(comment or letter or editorial or note or erratum or short survey or news or newspaper article or patient education handout or case report or historical article).pt.(1986428)	humans/(11060548)
24	22 not 23(1002)	22 not 23(506080)
25	limit 24 to english(817)	21 not 24(1504)
26	animals/(5564286)	limit 25 to yr="2000 -Current"(1454)
27	humans/(14304076)	
28	26 not 27(4001326)	
29	25 not 28(798)	
30	limit 29 to yr="2000 -Current"(512)	
31	remove duplicates from 30(496)	

[a] In-process and other non-indexed citations, and 1946 to present.
[b] 1996 to 2015 Week 35.

TABLE II Summary of the studies assessing follow-up care for asymptomatic survivors of lymphoma who received curative-intent treatment

Study (country)	Aim	Population and post-treatment follow-up	Intervention	Patients included (*n*)	Outcome reported
Dryver *et al.*, 2003[4] (Canada)	To evaluate the utility of the clinical assessments, radiologic tests, and laboratory tests to detect a Hodgkin relapse	Patients with Hodgkin lymphoma relapse after initial curative therapy Follow-up[a]: ■ Clinical evaluation ■ Imaging	Clinical symptoms vs. imaging detection vs. laboratory testing	68 (109 suspected relapses)	Relapse detection (proportion) by mode of detection: ■ Patient ■ Physician ■ Imaging ■ Lab test
Liedtke *et al.*, 2006[5] (U.S.A.)	Evaluate the role of surveillance imaging in detection of relapsed disease and its impact on outcomes of salvage treatment	Patients with biopsy-confirmed relapse of aggressive NHL Follow-up: ■ Surveillance imaging (no further details reported)	Unscheduled imaging or clinical symptoms vs. routine imaging (unscheduled imaging occurring because of self-reported symptoms or new physical examination, or abnormal findings on routine exam)	108 (24 routine imaging, 84 unscheduled imaging)	■ Relapse detection (proportion) ■ Scans (*n*) per relapse detected ■ Progression-free survival ■ Overall survival rate
Goldschmidt *et al.*, 2011[6] (Israel)	Describe the diagnostic modality by which relapse was detected and evaluate whether the use of PET/CT influenced survival rate in patients with relapsed Hodgkin lymphoma or aggressive NHL	Patients >18 years at diagnosis of Hodgkin lymphoma or aggressive NHL (DLBCL, peripheral T-cell lymphoma, Burkitt lymphoma, lymphoblastic lymphoma) who relapsed at least 1 month after achieving first CR Follow-up[a]: ■ Clinical evaluation ■ Imaging	Clinical detection vs. imaging detection	125 (42 Hodgkin lymphoma, 83 aggressive NHL)	■ Proportion of relapse detection ■ Overall survival rate
Lin *et al.*, 2012[7] (Taiwan)	Describe the value of surveillance CT in the detection of disease relapse in patients with DLBCL and FL3, and evaluate whether relapse detected by various methods influences outcome	Patients with DLBCL and FL3 in CR or with unconfirmed CR Follow-up[a]: ■ Physical examination and laboratory evaluation ■ Surveillance CT	Relapse detection: clinical vs. surveillance CT	341 (314 DLBCL, 27 FL3)	■ Proportion of relapse detection ■ Mean time from latest normal CT to relapse ■ Scans (*n*) per relapse detected ■ Mean interval of surveillance CT ■ Mean CT scans (*n*) per year
Cheah *et al.*, 2013[8] (Australia)	Assess the role of PET/CT imaging in the surveillance of patients achieving CR after primary therapy for DLBCL	Patients with DLBCL in CR after primary therapy who underwent PET-CT imaging. Follow-up[a]: ■ Surveillance imaging	Surveillance imaging: symptomatic vs. asymptomatic	116 (450 surveillance PET/CT scans)	■ Overall post-relapse survival rate

TABLE II Continued

Study (country)	Aim	Population and post-treatment follow-up	Intervention	Patients included (*n*)	Outcome reported
Dann *et al.*, 2013[9] (Israel, New Zealand)	Evaluate the effectiveness of follow-up imaging in Hodgkin lymphoma using PET/CT or CT as a routine mode of surveillance in addition to dedicated imaging if relapse is suspected compared with clinical follow-up and dedicated imaging performed upon suspicion of relapse	International multicentre study involving adult patients (>18 years of age at diagnosis) treated with curative intent who achieved a CR, some unconfirmed, managed at 2 Israeli centres (Rambam Health Care Campus in Haifa, and Hadassah-Hebrew University Medical Centre in Jerusalem) and at 1 N.Z. academic centre (Auckland Medical Centre in Auckland) Arm 1 follow-up[a]: ■ Clinical surveillance Arm 2 follow-up[a]: ■ Imaging surveillance	Clinical surveillance vs. imaging surveillance	368 (291 in Israel, 77 in New Zealand)	■ Median time to relapse ■ Hazard ratio for follow-up mode ■ Relapse detection rate ■ Scans (*n*) per relapse ■ Scans (*n*) per patient to detect relapse ■ Progression-free survival rate
Hong *et al.*, 2014[10] (South Korea)	Assess the role of routine imaging and of symptom-directed unplanned early outpatient department visits in patients with DLBCL	Adult patients (≥20 years) with DLBCL in CR as demonstrated by FDG-PET/CT who had at least 1 outpatient department visit for relapse monitoring. Follow-up[a]: ■ Outpatient department visits	Planned visits vs. unplanned visits	106 (856 visits)	■ Relapse detection rate ■ Overall survival rate (from initial therapy and from relapse)
Pingali *et al.*, 2014[11] (U.S.A.)	Compare the outcomes of patients with classical Hodgkin lymphoma who underwent either routine surveillance imaging or clinical surveillance	Adult patients newly diagnosed at 3 participating academic tertiary care medical centres, who achieved a CR confirmed by CT, PET, or both at the end of the first-line therapy. Arm 1 follow-up: ■ Imaging surveillance ■ History, physical examination, laboratory studies ■ Surveillance imaging by CT, PET, or both before the follow-up visit Arm 2 follow-up: ■ Clinical surveillance ■ History, physical examination, and laboratory studies ■ Imaging was obtained only to evaluate concerning signs or symptoms of relapse	Clinical surveillance vs. imaging surveillance	241	■ 5-Year overall survival ■ 5-Year incidence of relapse ■ Median time to detect relapse ■ Scans (*n*) per relapse detected ■ Scan rate
Truong *et al.*, 2014[12] (U.S.A.)	Determine the value of routine imaging for detecting relapse in patients with NHL in CR after first-line therapy	Patients with NHL in CR Follow-up[a]: ■ Clinician visits, laboratory analysis ■ Imaging surveillance	Clinical surveillance vs. imaging surveillance	1086 with lymphoid malignancies	■ Proportion of relapse detection ■ Overall survival rate

TABLE II Continued

Study (country)	Aim	Population and post-treatment follow-up	Intervention	Patients included (*n*)	Outcome reported
El-Galaly *et al.*, 2015[13] (Denmark, Sweden)	Compare the survival rates of patients with DLBCL in Denmark and Sweden (countries with similar health care systems, but completely different standards for routine imaging)	Patients from population-based lymphoma registries [Danish Lymphoma Group Registry (LYFO) and the Swedish Lymphoma Registry (SLR)] that cover ≥90% of adult patients with lymphoma in Denmark and Sweden LYFO follow-up[a]: ■ Clinical visits ■ Routine imaging SLR follow-up[a]: ■ Clinical visits ■ Imaging only if relapse is clinically suspected	National follow-up policy for patients with DLBCL in CR	1221 (525 LYFO, 696 SLR)	■ Overall survival rate
Thompson *et al.*, 2015[14] (U.S.A., France)	Assess the utility of post-therapy surveillance imaging in a cohort of patients with DLBCL from the United States and confirm the results in an independent cohort of patients from France	Two cohorts of patients with DLBCL in CR who received anthracycline-based immunochemotherapy as initial therapy MER cohort: patients identified from the Molecular Epidemiology Resource (MER) in the United States Lyon cohort: patients identified from the León Bérard Cancer Centre, Lyon, France. MER cohort follow-up[a]: ■ Clinical visits (no details reported for imaging) Lyon cohort follow-up[a]: ■ Clinical visits ■ Surveillance CT imaging	Before scheduled visits vs. scheduled visits	—	■ Overall survival rate ■ Median time to relapse (in patients diagnosed with asymptomatic DLBCL relapse by imaging)

[a] See Table V for detailed follow-up schedule.

NHL = non-Hodgkin lymphoma; PET = positron-emission tomography; CT = computed tomography; DLBCL = diffuse large B-cell lymphoma; CR = complete remission; FL3 = grade 3 follicular lymphoma; FDG = fluorodeoxyglucose.

Table III presents a description of the study designs and the quality of the studies. Overall, the body of evidence is limited mainly by designs based on retrospective analyses of electronic medical records and by relatively small sample sizes with a low number of relapses. The sample size of the included studies ranged from a low of 109 to a high of 1221 in a population-based study comparing the survival rate of patients with lymphoma undergoing different clinical follow-up policies[4,13]. In most of the studies, patients had NHL[5,7,8,10,12–14]; three studies focused on the follow-up of patients with Hodgkin lymphoma[4,9,11], and one study reported on patients with both types of lymphoma[6]. The number of relapses ranged from a low of 15 to a high of 163 in patients with NHL[10,12], and from a low of 11 to a high of 42 in patients with Hodgkin lymphoma[6,11].

Outcomes

Clinical Activities for Detecting Recurrence

Table IV summarizes the clinical activities used for detection of clinical recurrence.

Detection of Relapse: Nine studies reported on the follow-up care of asymptomatic survivors of lymphoma who had received curative-intent treatment[4–12]. Two studies involving patients with NHL in complete remission detected a statistically significant difference in the number of relapses initially suspected by clinical manifestations (patient-reported symptoms or physical examination) compared with relapses initially suspected by imaging before clinical manifestation[10,12]. The study reported by Hong *et al.*[10] assessed the role of routine imaging compared with symptom-directed unplanned early outpatient department visits in patients with DLBCL and reported that, compared with planned visits with or without clinical symptoms or signs, early visits because of symptoms or signs have a strong association with the detection of relapse (33% vs. 0.5%, $p < 0.001$). Similarly, the study reported by Truong *et al.*[12] found that, for most relapses in aggressive NHL, patient-reported symptoms led to detection (86% vs. 14%, $p < 0.0001$).

Two additional studies in patients with NHL detected that the proportion of relapses initially suspected by clinical manifestations ranged from a low of 54%[8] to a high of 78%[5,7] and that the proportion of relapses initially suspected by surveillance imaging ranged from a low of 22%[5,7] to a high of 46%[8].

Three studies involved patients with Hodgkin lymphoma[4,9,11]. The study reported by Pingali *et al.*[11] compared the incidence of relapse in patients managed with clinical surveillance alone and in those who underwent routine surveillance imaging, reporting that differences between groups were not statistically significant (7.4% vs. 3.4%, $p = 0.39$). The two remaining studies reported that the proportion of relapses initially suspected by clinical manifestations ranged from a low of 13%[9] to a high of 64%[4] and that the proportion of relapses initially suspected by surveillance imaging ranged from a low of 8%[9] to a high of 27%[4].

Overall Survival: Seven studies reported on overall survival outcomes[5,8,10–14]. Six of the studies reported comparable survival rates for patients with relapse initially detected by clinical manifestations and initially detected by surveillance imaging[5,8,11–14].

The study reported by Hong *et al.*[10] found a median time from relapse to death of 6.7 months and an overall survival time of 38.3 months for 11 patients with relapse initially detected by early unplanned visits (clinical manifestations); however, determining whether routine imaging can prolong the survival of relapsed patients was not possible because of the small number of patients ($n = 4$) with relapse initially detected by planned visits with ($n = 3$) or without routine imaging ($n = 1$). Of those patients with relapse, the 3 whose relapses were detected at planned visits with imaging had times from relapse to death of 5.7, 7.9, and 9.0 months and overall survival times of 17.1, 18.9, and 50.2 months. For the 1 patient with relapse detected at a planned visit without routine imaging, the time from relapse to death was 7.6 months, and the overall survival time was 51.9 months.

Time to Relapse: Four of the studies reported time to relapse[7,9,11,14]. Only the study reported by Lin *et al.*[7] detected a significant benefit for patients with first presentation of relapse found by clinical manifestations than for patients with asymptomatic relapse found by surveillance imaging (mean: 4.5 months vs. 6.0 months, $p = 0.042$). The study conducted by Thompson *et al.*[14] reported median times of 19 and 11 months from diagnosis to relapse in cohorts of asymptomatic patients from the United States and France respectively; the median times from diagnosis to relapse in patients with clinical manifestations of relapse were not reported. The study conducted by Dann *et al.*[9] reported a median time to relapse of 8.6 months both for patients undergoing routine clinical follow-up and for patients undergoing routine clinical follow-up with routine imaging. Pingali *et al.*[11] reported median times to relapse of 33 and 18 months in patients with Hodgkin lymphoma whose relapses were initially suspected by clinical manifestations and by imaging respectively.

Frequency of Imaging: Three studies reported on frequency of imaging[7,9,11]. Two of the studies found that, compared with clinical surveillance, routine surveillance imaging in patients with Hodgkin lymphoma was statistically significantly associated with a higher number of scans. Dan *et al.*[9] reported that, with routine imaging follow-up, 47.5 studies were required to detect a single relapse; clinical follow-up required 4.7 imaging studies. In the routine imaging follow-up arm, 3.9 imaging studies per patient were required; in the clinical follow-up arm, 0.6 studies per patient were required ($p < 0.001$). Similarly, the study conducted by Pingali *et al.*[11] reported that the imaging rate in the routine imaging surveillance group was greater by a factor of 4.5 than the rate in the clinical surveillance group (0.89 vs. 0.21, $p < 0.0001$); the number of scans per relapse detected was 127 in the routine imaging surveillance arm; it was 14.6 scans in the clinical surveillance group.

No statistically significant differences by follow-up were reported in a study of patients with NHL by Lin *et al.*[7]. The average number of scans per patient was 3.2 in both

TABLE III Quality assessment for included studies

Reference (country)	Lymphoma type	Relapsing survivors (*n*)	Outcome criteria	Recruitment method	Comparison type	Intervention	Funding source	Comments
Dryver *et al.*, 2003[4] (Canada)	Hodgkin lymphoma	68 (109 suspected relapses)	Clinically suspected vs. imaging suspected	Single centre: Toronto Sunnybrook Regional Cancer Centre, Toronto, ON	Follow-up groups	Clinical symptoms vs. routine imaging vs. laboratory test	Not reported	
Liedtke *et al.*, 2006[5] (U.S.A.)	Aggressive NHL	Not reported	Clinically suspected by routine imaging vs. unscheduled imaging	Single institution: Memorial Sloan Kettering Cancer Center, New York, NY, U.S.A.	Follow-up groups	Routine imaging vs. clinical symptoms (patient-reported symptoms or findings on routine exam)	A fellowship from the Lymphoma Research Foundation	As part of salvage therapy (2nd-line therapy), 88 patients underwent SCT
Goldschmidt *et al.*, 2011[6] (Israel)	Hodgkin lymphoma, aggressive NHL (DLBCL)	Not reported	Clinically suspected vs. imaging findings	Single institution: Hadassah-Hebrew University Medical Centre, Jerusalem, Israel	Follow-up groups	Clinical surveillance vs. imaging surveillance	Not reported	As part of salvage therapy (2nd-line therapy), 47 patients underwent SCT
Lin *et al.*, 2012[7] (Taiwan}	DLBCL and FL3	341	Imaging-detected relapses: asymptomatic vs. symptomatic	Single institution: Chang Gung Memorial Hospital, Taipei, Taiwan	Follow-up groups	Imaging surveillance vs. clinical symptoms	Grant from Department of Health, Taiwan (no. DOH99-TD-C-111-006)	Study population included 21 patients with unconfirmed CR (8 in the imaging group and 13 in the clinical/symptomatic group); as part of salvage therapy (2nd-line therapy), 16 patients underwent SCT
Cheah *et al.*, 2013[8] (Australia)	DLBCL	116	Symptomatic relapses vs. asymptomatic relapses	Single institution: Peter MacCallum Cancer Centre, Melbourne, Australia	Symptomatic vs. asymptomatic	Imaging surveillance vs. clinical symptoms	Grant from the Victoria Cancer Agency and a New Investigator Scholarship awarded by the Haematology Society of Australia and New Zealand	As part of salvage therapy (2nd-line therapy), 7 patients underwent SCT
Dann *et al.*, 2013[9] (Israel, New Zealand)	Classical Hodgkin lymphoma	368 (63 clinical, 305 imaging)	Relapses suspected by clinical follow-up vs. imaging	Three medical centres: Rambam Health Care Campus, Haifa, Israel; Hadassah-Hebrew University Medical Centre, Jerusalem, Israel; and Auckland Medical Centre, Auckland, New Zealand	Follow-up groups	Imaging surveillance vs. clinical surveillance	Not reported	The imaging group included 14 patients with unconfirmed CR

TABLE III Continued

Reference (country)	Lymphoma type	Relapsing survivors (*n*)	Outcome criteria	Recruitment method	Comparison type	Intervention	Funding source	Comments
Hong *et al.*, 2014[10] (South Korea)	—	106 [856 outpatient department visits (823 planned, 33 unplanned)]	Relapses suspected by routine imaging vs. clinical signs or unplanned early visit	Single institution: Gachon University Gil Medical Center, Incheon, South Korea	Follow-up groups	Planned outpatient department visits vs. unplanned early visit because of abnormal symptoms or signs	Not reported	As consolidative therapy, 7 patients underwent autologous SCT
Pingali *et al.*, 2014[11] (U.S.A.)	Classical Hodgkin lymphoma	241 (174 imaging, 67 clinical)	Relapses suspected by routine imaging vs. clinical surveillance	Three academic tertiary care medical centres: Medical College of Wisconsin, Milwaukee, WI, U.S.A.; University of Nebraska Medical Center, Omaha, NE, U.S.A.; and Washington University School of Medicine, St. Louis, MO, U.S.A.	Follow-up groups	Imaging surveillance vs. clinical surveillance	The Donald J. Schuenke Cancer Fellowship	As part of the salvage therapy (2nd-line therapy), all but 1 relapsed patient underwent autologous SCT
Truong *et al.*, 2014[12] (U.S.A.)	NHL	1086	Relapses suspected by clinical follow-up vs. surveillance imaging	Single institution: Osborn Hematopoietic Malignancy and Transplantation Program, West Virginia University, Morgantown, WV, U.S.A.	Follow-up groups	Imaging surveillance vs. clinical surveillance	Not reported	
El-Galaly *et al.*, 2015[13] (Denmark, Sweden)	DLBCL	1221 (525 LYFO; 696 SLR)	Routine follow-up with imaging vs. routine follow-up without imaging (Denmark vs. Sweden)	Two population-based registries: Danish Lymphoma Group Registry (LYFO) and Swedish Lymphoma Registry (SLR)	National follow-up policies	Policies followed by Sweden vs. Denmark	Not reported	The number of people who actually underwent imaging in each country was not validated; the results from this study therefore refer to differences in follow-up policies between Sweden and Denmark
Thompson *et al.*, 2015[14] (U.S.A., France)	DLBCL	U.S.A. (MER): 552 France (Lyon): 261	Relapses suspected because of symptoms vs. relapses detected at scheduled visits	Two centres: Molecular Epidemiology Resource (MER) of the University of Iowa and Mayo Clinic Lymphoma Specialized Program of Research Excellence, Iowa City, IA, U.S.A.; and Léon Bérard Cancer Center, Lyon, France	Follow-up groups	Scheduled visits vs. unscheduled visits	The Lymphoma SPORE (CA P50 CA97274), Predolin Foundation, Mayo Clinic Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery, and the Arnold and Kit Palmer Benefactor Award	

NHL = non-Hodgkin lymphoma; SCT = stem-cell transplantation; DLBCL = diffuse large B-cell lymphoma; FL3 = follicular lymphoma grade 3; CR = complete remission; MER = Molecular Epidemiology Resource.

TABLE IV Clinical activities for detection of clinical recurrence or further hematologic neoplasms in asymptomatic survivors of lymphoma who received curative-intent treatment

Reference (study period)	Population	Median follow-up	Sample size (*n*)	Relapse detection		Outcomes
				(*n*)	Method	
Dryver *et al.*, 2003[4] (1990–1999)	Patients with Hodgkin lymphoma relapse	38 Months (range: 1–120 months)	68 (109 suspected relapses) Suspected by: patient, 46; physician, 28; imaging, 31; lab test, 4	22 True relapses	Clinical symptoms: 14 (10 patient concern, 4 physician concern) Routine imaging: 6 (4 chest radiography, 2 routine CT) Laboratory test: 2	Proportion of relapses detected (%): clinical symptoms, 64 (patient concern, 46; physician concern, 18); routine imaging, 27% (chest radiography, 18; routine CT, 9); laboratory test: 9; *p*=NR
Liedtke *et al.*, 2006[5] (1993–2000)	Patients with biopsy-confirmed relapse of aggressive NHL	5 Years	NR	108	Clinical symptoms: 84 (self-reported, 78; routine exam, 6) Routine imaging: 24 *Note:* 73 of the 84 clinical relapses were detected by unscheduled imaging because of patient-reported symptoms or abnormal findings on exam. It is not clear how the other 11 relapses were detected or confirmed.	Proportion of relapses detected (%): routine imaging, 22; unscheduled imaging, 78; *p*=NR Scans (*n*) per relapse detected: routine imaging, 3.5; unscheduled imaging, 2.0; *p*=NR Progression free survival (months): routine imaging, 34; unscheduled imaging, 11; *p*=0.12 5-Year overall survival (%): routine imaging, 54; unscheduled imaging, 43; *p*=0.13
Goldschmidt *et al.*, 2011[6]	Patients with Hodgkin lymphoma or aggressive NHL in CR	Not reported	208 (42 Hodgkin lymphoma, 83 aggressive NHL, 81 DLBCL, 1 peripheral T-cell, 1 lymphoblastic leukemia)	125	Clinical: 78 (20 Hodgkin lymphoma; 58 aggressive NHL) Routine imaging: 47 (22 Hodgkin lymphoma; 25 aggressive NHL)	Proportion of relapse detection overall (%): clinical, 62; imaging, 38 Proportion of relapse detection for Hodgkin lymphoma (%): clinical, 16; imaging, 17.6 Proportion of relapse detection for aggressive NHL (%): clinical, 46.4; imaging, 20
Lin *et al.*, 2012[7] (2003–2009)	Patients with DLBCL or FL3	Not reported	341	113 (DLBCL, 314; FL3, 27)	Clinical: 88 (DLBCL, NR; FL3, NR) Routine imaging: 25 (DLBCL, 22; FL3, 3)	Proportion of relapse detection (%): clinical, 78; routine imaging: 22; *p*=NR Mean time from latest normal CT to relapse (months): clinical, 4.5; routine imaging, 6.0; *p*=0.042 Scans (*n*) per relapse detected: clinical, 3.2; routine imaging, 3.2; *p*=0.749 Mean interval between surveillance CT imaging tests (months): clinical, 4.8; routine imaging, 4.4; *p*=0.473 Mean CT imaging tests per year (*n*): clinical, 2.3; routine imaging, 2.4; *p*=0.423
Cheah *et al.*, 2013[8] (2002–2009)	Patients with DLBCL and PET/CT imaging	53 Months (range: 8–133 months)	116 (450 surveillance PET/CT scans)	13	Symptomatic: 7 (54%) Asymptomatic: 6 (46%)	Overall survival after relapse: *p*=0.76

TABLE IV Continued

Reference (study period)	Population	Median follow-up	Sample size (*n*)	Relapse detection		Outcomes
				(*n*)	Method	
Dann *et al.*, 2013[9] (2001–2010)	Patients with Hodgkin lymphoma in CR	Clinical: 43 months Clinical/imaging: 63 months	368 [63 in New Zealand for whom imaging was performed only if suspicions for relapse; 305 for whom routine imaging (PET/CT or CT) was performed; 292 at Israeli centres, 13 at the N.Z. academic centre because of the presence of a residual mass at the end of treatment (unconfirmed CR)]	33	Clinical: 8 Imaging: 25 (routine imaging, 17; dedicated imaging because of clinical suspicion or inconclusive PET/CT, 8)	Median time to relapse (months): clinical, 8.6 (95% CI: 1.3 to 15.8); imaging, 8.6 (95% CI: 7 to 10) Hazard ratio for follow-up mode: 0.6 (95% CI: 0.3 to 1.5); p=0.32 3-Year relapse detection rate (%): clinical, 13; imaging, 8 (routine imaging, 6; imaging because of clinical suspicion, 6); p=NR Scans (*n*) per relapse detected: clinical, 4.75; imaging, 47.5 p=NR Imaging tests per patient to detect relapse: clinical, 0.6; imaging, 3.9; p<0.001 3-Year progression-free survival (%): clinical, 86; imaging, 93; p=NS
Hong *et al.*, 2014[10] (May 2004–Feb 2012)	Patients with DLBCL in CR	30 Months	106 [856 outpatient department visits (median: 6 visits; range: 1–25 visits)] Planned routine visits: 823 (imaging, 501; without imaging, 322) Unplanned early visits: 33 (because of abnormal symptoms)	15	Planned visits: 4 Unplanned visits: 11	Relapse detection rate (%): planned visits, 0.5; unplanned visits, 33; p<0.001 Overall survival from initial therapy (months): planned visits, not calculated (small number of relapses); unplanned visits, 38.3 (95% CI: 31.1 to 45.5) Overall survival from relapse (months): planned visits, not calculated (small number of relapses); unplanned visits, 6.7 (95% CI: 3.0 to 10.3)
Pingali *et al.*, 2014[11] (Jan 2000–Dec 2010)	Adult patients with classical Hodgkin lymphoma in CR after first-line therapy	Imaging: 4.1 Years (range: 0.3–10.7 years) Clinical: 4.5 Years (range: 0.4–10.6 years) p=0.12	241 (imaging, 174; clinical, 67)	11 (imaging, 6; clinical, 5)		5-Year overall survival (%): clinical, 96 (95% CI: 86 to 99); imaging, 97 (95% CI: 92 to 99); p=0.41 5-Year incidence of relapse (%): clinical, 7.4; imaging: 3.4; p=0.39 Median time to relapse (months): clinical, 33; imaging, 18; p=NR Scans (*n*) per relapse detected: clinical, 14.6; imaging, 127; p=NR Scan rate (%): 4.5 (95% CI: 3.1 to 5.5); Scans per year: clinical, 0.21; imaging, 0.98; p<0.0001
Truong *et al.*, 2014[12] (2000–2010)	Patients with lymphoid malignancies	24 Months (range: 1–157 months)	1086	84	Clinical: 72 (because of patient-reported symptoms or physical examination) Imaging: 12	Proportion of relapse detection (%): clinical, 86; imaging, 14; p<0.0001 Overall survival: method of detecting relapse had no effect, p=0.77
El-Galaly *et al.*, 2015[13] (2007–2012)	Patients with DLBCL in CR	51 Months	1221 (Danish Lymphoma Group Registry, 525; Swedish Lymphoma Registry, 696)	NA		3-Year overall survival (%): Danish, 92; Swedish, 91; p=0.7

TABLE IV Continued

Reference (study period)	Population	Median follow-up	Sample size (*n*)	Relapse detection		Outcomes
				(*n*)	Method	
Thompson *et al.*, 2015[14] (2002–2009)	Patients with DLBCL in CR	United States (MER): 71 months (range: 6–129 months)	MER cohort: 552	MER: 85	63 Before scheduled visit because of symptoms; 22 after scheduled visit (clinical features, 13; routine imaging, 9)	Overall survival, DLBCL relapses (months): before scheduled visit, 15 (95% CI: 8 to 26); scheduled visits, 21 (95% CI: 11 to 57); p=0.56 Median time to DLBCL relapse detected by imaging (months): 19 (95% CI: 8 to 46)
		León Bérard Cancer Centre, Lyon, France: 77 months (range: 5–162 months)	Lyon cohort: 222	Lyon: 55	28 Before scheduled visit because of symptoms; 18 after scheduled visit (clinical features, 14; routine imaging, 4)	Overall survival, DLBCL relapses (months): before scheduled visit, 12 (95% CI: 3 to 22); scheduled visits, 19 (95% CI: 3 to 82); p=0.25 Median time to DLBCL relapse detected by imaging (months): 11 (95% CI: 7 to 16)

CT = computed tomography; NR = not reported; NHL = non-Hodgkin lymphoma; CR = complete remission; DLBCL = diffuse large B-cell lymphoma; FL3 = follicular lymphoma grade 3; PET = positron emission tomography; CI = confidence interval; NS = nonsignificant; NA = not applicable; MER = Molecular Epidemiology Resource.

the routine surveillance imaging arm and the arm in which relapse was detected by clinical manifestations (p = 0.749); the mean number of scans per year was reported to be 2.3 for routine surveillance imaging and 2.4 for clinical manifestations (p = 0.423).

Frequency and Timing of Clinical Activities for Detecting Recurrence

The literature search did not return any study specifically designed to evaluate the effectiveness of various frequencies and timings of follow-up for asymptomatic survivors of lymphoma who had received curative-intent treatment. However, the nine studies that were discussed while addressing research question 1 (effective clinical strategies) provided the follow-up schedules used by the institutions from which each population was selected and the relationship of those schedules with relapse detection (full description in Table v). Eight of the studies described follow-up schedules used by single institutions[4,6–10,12,14]. The study reported by El-Galaly *et al.*[13] described the follow-up schedules used by two neighbouring Scandinavian countries with similar health care systems (Denmark and Sweden), but completely different traditions for routine imaging. Most studies reported performing clinical follow-up every 2–3 months for the first 2 years, and then every 4–6 months in the subsequent 3 years (years 3–5), with annual visits thereafter. Surveillance imaging was performed mainly for patients in whom relapse was suspected.

Surveillance Procedures for Detecting Therapy-Related Secondary Malignancies

The literature search did not return any study specifically designed to evaluate follow-up schedules for detecting therapy-related secondary malignancies in asymptomatic survivors of lymphoma who had received curative-intent treatment. Documentation of therapy-related secondary malignancies might be more available in the radiation safety literature rather than in the lymphoma diagnosis and follow-up literature.

DISCUSSION

There is accumulating descriptive literature suggesting that patients with lymphoma treated with curative intent who achieve complete remission might not benefit from routine surveillance with diagnostic imaging. Currently, routine surveillance protocols, often informed by clinical trials protocols and local practice culture, include history, physical examination, blood tests, and imaging. Surveillance investigations are based on the presumption that early detection of recurrence might improve the outcomes of patients in complete remission because of a higher likelihood of successful response to salvage therapy when the clinical burden is lower. It is also recognized that certain therapies can be associated with a predictable incidence of late organ adverse effects such as heart disease or second cancers, and some routine testing is directed toward monitoring the development of such complications. In the present review, we sought to examine the evidence for surveillance and toxicity screening in this population of interest.

TABLE V Frequency and timing of clinical activities for detecting clinical recurrence or further hematologic neoplasms in asymptomatic survivors of lymphoma who received curative-intent treatment

Reference (country)	Follow-up	
	Protocol	**Frequency**
Dryver *et al.*, 2003[4] (Canada)	Clinical visits: clinical assessment (history and physical), chest radiography, complete blood count	■ Every 3 months for the first 2 years ■ Every 6 months for years 3–5 ■ Annually from year 5 onward
	Surveillance imaging	■ At the discretion of the treating physician ■ Radiography conducted during the clinical visits
Goldschmidt *et al.*, 2011[6] (Israel)	Clinical visits	■ Every 3–4 months for the first 2 years ■ Every 6 months for years 3–5 ■ Annually from year 5 onward
	Surveillance imaging (CT, PET, or PET/CT)	■ Every 6 months for the first 2 years ■ Once at end of year 3
Lin *et al.*, 2012[7] (Taiwan)	Clinical visits and laboratory analysis (blood count with differential, serum lactate dehydrogenase, and serum β_2-microglobulin)	■ Every 1–3 months for the first 2 years
	Surveillance imaging (by CT) routinely performed (head, neck, chest, abdomen, and pelvis)	■ Every 3–6 months or when clinically indicated for the first 2 years ■ Annually or when clinically indicated for years 3–5
Cheah *et al.*, 2013[8] (Australia)	Surveillance imaging (PET/CT)	■ Every 6 months for the first 2 years ■ Annually for years 3–5
Dann *et al.*, 2013[9] (Israel, New Zealand)	Arm 1: Clinical surveillance	■ Every 3–4 months for the first 3 years ■ Every 6 months for years 4–5 Imaging only when clinical findings are suspicious for relapse
	Arm 2: Imaging surveillance (clinical surveillance and imaging)	■ Every 6 months for the first 2 years ■ Once in year 3
Hong *et al.*, 2014[10] (South Korea)	Clinical visits: history, physical, complete blood count	■ Every 2–3 months for the first 2 years ■ Every 4–6 months for years 3–5 ■ Annually from year 5 onward
	Imaging (CT or FDG-PET/CT)	■ At discretion of the attending physician
Truong *et al.*, 2014[12] (U.S.A.)	Clinical visits and laboratory analysis	■ Every 3–4 months for the first 2 years ■ Every 6 months for years 3–5 ■ Annually from year 5 onward
	Surveillance imaging (PET/CT or CT) routinely performed	■ Every 4 months for the first year ■ Every 6 months in year 2 ■ Annually for years 3–5
El-Galaly *et al.*, 2015[13] (Denmark, Sweden)	Clinical visits: symptom assessment, clinical examination, blood test	Denmark: ■ Every 3 months for the first 2 years ■ Every 6 months for years 3–5 Sweden: ■ Every 3–4 months for the first 2 years ■ Every 6 months for year 3 ■ Annually for years 4–5
	Surveillance imaging (by CT): neck, thorax, abdomen	Denmark: ■ Every 6 months for the first 2 years According to a survey of attending lymphoma specialists from 6 large Danish hematology centres, all hematologists prescribed routine CT imaging during the first 2 years of follow-up: ■ Every 6 months for 2 years: 94% ■ Annually for 1 or 2 years: 6% ■ Prescribe CT after the 2nd year of follow-up: 15% Sweden: ■ Only if relapse is clinically suspected In Sweden, routine imaging for DLBCL in CR is discouraged by the national guidelines, and in a survey of the 10 major hematology/oncology centres covering >90% of the total Swedish lymphoma population, all centres reported adherence to the guidelines

TABLE V Continued

Reference (country)	Follow-up	
	Protocol	**Frequency**
Thompson *et al.*, 2015[14] (U.S.A., France)	Clinical visits	U.S.A. (MER cohort): ■ Every 6 months for the first 3 years ■ Annually from year 3 onward France (Lyon cohort): ■ Every 3 months for the first 2 years ■ Every 6 months for years 3–5 ■ Annually from year 5 onward
	Surveillance imaging (by CT)	U.S.A. (MER cohort): ■ Not reported France (Lyon cohort): ■ At 6 and 12 months in year 1 (frequency of CT imaging adapted to the initial stage and prognostic score)

CT = computed tomography; PET = positron-emission tomography; DLBCL = diffuse large B-cell lymphoma; CR = complete remission; MER = Molecular Epidemiology Resource.

Currently, no Canadian consensus document sets out the optimal follow-up care for asymptomatic survivors of lymphoma who have received curative-intent treatment. The present evidence summary was framed by three areas of inquiry: clinical activities to detect relapse, frequency and timing of clinical activities to detect relapse, and activities to detect therapy-related secondary malignancies in survivors of lymphoma.

Eleven retrospective studies that specifically reported on surveillance activities to detect recurrence were identified. Complete remission was defined mainly by computed tomography imaging criteria. In most studies, a planned imaging approach, most often using computed tomography, was compared with imaging performed in response to signs and symptoms. The study populations included aggressive-histology NHL and Hodgkin lymphoma stages I–III. No prospective comparisons were found. In all studies, no significant differences in survival—our key outcome of interest—were found between planned and unplanned visits. Unfortunately, given that all nonrandomized studies carry an unclear risk of bias, the quality of the evidence supporting that summary is low.

Consistent evidence is lacking to support routine imaging surveillance in survivors of lymphoma who were treated with curative intent and who were considered to be in remission at the completion of all planned therapy. It was noted in many of the studies that, even in the planned surveillance arms, most relapses were detected in the interval between planned imaging appointments and were most often initiated by signs and symptoms reported by patients.

We also reviewed the clinical visit schedules reported in the trials. In nine studies, the timing of clinical visits was described. We were unable to find any studies that compared routine clinical visits with visits only in response to symptoms, nor any comparisons of the use of routine blood work compared with blood work at the discretion of the treating oncology team, and therefore no clinical visit schedule was described.

Most of the studies reported clinical follow-up every 2–3 months for the first 2 years, and then every 4–6 months for the following 3 years (years 3–5), with annual visits thereafter. Surveillance imaging was performed mainly in cases of suspected relapse. Most relapses are recognized to occur in the first 2–3 years after completion of therapy, and that recognition is reflected in a clinical visit pattern that is fairly consistent from study to study. The pattern is similar to that described in the 2015 National Comprehensive Cancer Network guideline[15]: follow-up of patients with Hodgkin lymphoma should be based mainly on interim history and physical examination; computed tomography imaging is acceptable once during the first 12 months and should be clinically prompted thereafter. Similarly, the 2015 National Comprehensive Cancer Network guideline[16] for patients with NHL recommends mainly clinical follow-up, with imaging only as clinically indicated for patients with DLBCL stages I and II, and no more often than every 6 months for the first 2 years and as clinically indicated afterward in patients with DLBCL stages III and IV. We cannot comment specifically on the added value of blood work in surveillance testing, but other reasons to monitor blood work might be present—particularly after chemotherapy, to assess for adverse effects. Frequency and timing continue to be at the discretion of the treating oncology team.

Finally, we are unable to comment on surveillance for second malignancies in survivors of treated lymphoma because no studies specifically addressing that issue were found. We recognize that population studies describing the risks of second malignancies such as breast cancer in young women treated with chest radiation can be considered in the development of follow-up guidelines.

SUMMARY

The evidence does not support the hypothesis of improved outcomes with routine diagnostic imaging in asymptomatic survivors of lymphoma who were treated for cure and were in complete remission at the end of planned treatment.

Prospective studies are required: first, to characterize the nature of follow-up visits as they are currently practiced; and subsequently, potentially to evaluate the multiple aspects of follow-up for this patient population. Such studies should address the components of a follow-up visit

that are of value from the perspective of both the health care system and the patients.

REVIEW PROCESS

This evidence summary was reviewed by the Director of the Program in Evidence-Based Care. It was also reviewed by Dr. Tom Kouroukis, Provincial Hematology Disease Site Lead at Cancer Care Ontario; Dr. Julian Dobranowski, Provincial Head of Cancer Care Ontario's Cancer Imaging Program; Dr. Blair Macdonald, Gastrointestinal and Genitourinary Radiologist at The Ottawa Hospital; and the members of the Hematology Cancer Disease Site Group, Cancer Care Ontario. The Working Group was responsible for ensuring that the necessary changes were made.

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CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology*'s policy on disclosing conflicts of interest, and we declare the following interests: The authors, members, and reviewers reported that they had no conflicts of interest. Nine authors declared no conflicts of interest, and two (JM, LH) declared conflicts. JM reported a potential conflict because, should lymphoma imaging indications become more liberal, his income as radiologist could potentially increase by more than $10,000. JM also declared that he had received $5,000 or more in a single year, plus other research support from Siemens, and he had been principal investigator for a clinical trial involving PET/MR studies. LH declared that she had been a co-principal investigator on a Canadian Institutes of Health Research–industry grant from Gilead Sciences. The interests as declared did not disqualify any individual from performing their designated role in the development of this evidence summary.

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