Guideline Endorsement 7-14 Version 3 REQUIRES UPDATING

A Quality Initiative of the Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

Endorsement of the 2018 American Society of Clinical Oncology Treatment of Malignant Pleural Mesothelioma Guideline

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An assessment conducted in November 2021 indicated that Guideline Endorsement 7-14 Version 3 REQUIRES UPDATING. It is still appropriate for this document to be available while this updating process unfolds. The PEBC has a formal and standardized process to ensure the currency of each document (PEBC Assessment & Review Protocol)

GL-END 7-14 Version 3 is comprised of 3 sections. You can access the full report here: https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/57556

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Endorsement of the 2018 American Society of Clinical Oncology Treatment of Malignant Pleural Mesothelioma Guideline

Section 1: Guideline Endorsement

GUIDELINE OBJECTIVE

The objective of this guideline is to provide recommendations on the most appropriate management of patients with malignant pleural mesothelioma. Our recommendations are based on the 2018 American Society of Clinical Oncology (ASCO) guideline on the treatment of malignant pleural mesothelioma.

TARGET POPULATION

This guideline targets adult patients with malignant pleural mesothelioma.

INTENDED USERS

The intended users of this guideline are medical, surgical, and radiation oncologists; oncology nurses and physician assistants; pulmonologists; radiologists; pathologists; and general practitioners managing patients with malignant pleural mesothelioma.

BACKGROUND INFORMATION

This Program in Evidence-Based Care (PEBC) guideline is an endorsement or adaptation of the ASCO treatment of malignant pleural mesothelioma guideline and is reprinted with permission [1] with the rationale included for any modifications.[1] The reader is referred to the ASCO systematic review [1] for additional information about the evidence. Any implementation considerations are listed.

PEBC RECOMMENDATIONS, JUSTIFICATION, AND IMPLEMENTATION CONSIDERATIONS

Recommendations are extracted from the ASCO recommendations.[1] The tables below include six adaptations to ASCO's recommendations, one removal, and nine implementation considerations.

Table 1-1. Recommendations of the American Society of Clinical Oncology guidelines for the treatment of malignant pleural mesothelioma: Diagnosis

Recommendation	Assessment
Recommendation 1.1: Clinicians should perform an initial thoracentesis when patients present with symptomatic pleural effusions and send pleural fluid for cytologic examination for initial assessment for possible mesothelioma (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	ENDORSED
Recommendation 1.2: In patients for whom antineoplastic treatment is planned, it is strongly recommended that a thoracoscopic biopsy should be performed. This will: (a) enhance the information available for clinical staging; (b) allow for histologic confirmation of diagnosis; (c) enable more accurate determination of the pathologic subtype of mesothelioma (epithelial, sarcomatoid, biphasic); and (d) make material available for additional studies (eg, molecular profiling) (Type of recommendation: evidence based; Evidence quality: high; Strength of recommendation: strong).	ENDORSED

Table 1-1. Recommendations of the American Society of Clinical Oncology guidelines for the treatment of malignant pleural mesothelioma: Diagnosis	
Recommendation	**Assessment**
Recommendation 1.2.1: When performing a thoracoscopic biopsy, the minimal number of incisions (two or fewer) is recommended and should ideally be placed in areas that would be used for subsequent definitive resection to avoid tumour implantation into the chest wall (Type of recommendation: evidence based; Evidence quality: high; Strength of recommendation: strong).	ENDORSED
Recommendation 1.3: In patients with suspected mesothelioma in whom treatment is planned, an open pleural biopsy should be performed if the extent of tumour prevents a thoracoscopic approach. The smallest incision possible is encouraged (generally 6 cm or less is recommended) (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: moderate).	ENDORSED
Recommendation 1.4: In patients who are not candidates for thoracoscopic biopsy or open pleural biopsy, who also have a nondiagnostic thoracentesis or do not have a pleural effusion, clinicians should perform a core needle biopsy of an accessible lesion (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	ENDORSED
Recommendation 2.0: Cytologic evaluation of pleural fluid can be an initial screening test for mesothelioma, but it is not a sufficiently sensitive diagnostic test. Whenever definitive histologic diagnosis is needed, biopsies via thoracoscopy or CT guidance offer a better opportunity to reach a definitive diagnosis (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	ENDORSED
Recommendation 3.0: Histologic examination should be supplemented by immunohistochemistry using selected markers expected to be positive in mesothelioma (eg, calretinin, keratins 5/6, and nuclear WT1) as well as markers expected to be negative in mesothelioma (eg, CEA, EPCAM, Claudin 4, TTF-1). These markers should be supplemented with other markers that address the differential diagnosis in that particular situation (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	ENDORSED
Recommendation 4.1: Mesothelioma should be reported as epithelial, sarcomatoid, or biphasic, because these subtypes have a clear prognostic significance (Type of recommendation: evidence based; Evidence quality: high; Strength of recommendation: strong).	ENDORSED
Recommendation 4.2: In surgical, thoracoscopic, or open pleural biopsies with sufficient tissue, further subtyping and quantification of epithelial versus sarcomatoid components of mesothelioma may be undertaken (Type of recommendation: informal consensus; Strength of recommendation: moderate).	ENDORSED
Recommendation 5.0: The non–tissue-based biomarkers that are under evaluation at this time do not have the sensitivity or specificity to predict outcome or monitor tumour response and are therefore not recommended (Type of recommendation: evidence-based; Evidence quality: intermediate; Strength of recommendation: moderate).	ENDORSED
Recommendation 6.0: While tumour genomic sequencing is currently done on a research basis in mesothelioma and it may become clinically applicable in the near future, it is not recommended at this time (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: moderate).	ENDORSED

Abbreviations: CEA, carcinoembryonic antigen; CT, computed tomography; EPCAM, epithelial cell adhesion molecule; TTF-1, thyroid transcription factor 1

Table 1-2. Recommendations of the American Society of Clinical Oncology guidelines for the treatment of malignant pleural mesothelioma: Staging	
Recommendation	**Assessment**
Recommendation 1.1: A CT scan of the chest and upper abdomen with IV contrast is recommended as the initial staging in patients with mesothelioma (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	ENDORSED
Recommendation 1.2: An FDG PET/CT should usually be obtained for initial staging of patients with mesothelioma. This may be omitted in patients who are not being considered for definitive surgical resection (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong). **Implementation considerations:** This may need to be reconsidered by the PET program at CCO as to whether it should be added to the list of approved indications.	ENDORSED with implementation considerations
Recommendation 1.3: If abnormalities that suggest metastatic disease in the abdomen are observed on a chest and upper abdomen CT or on a PET/CT then consideration should be given to perform a dedicated abdominal (1/2 pelvic) CT scan, preferably with IV and oral contrast (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	ENDORSED
Recommendation 1.4: An MRI (preferably with IV contrast) may be obtained to further assess invasion of the tumour into the diaphragm, chest wall, mediastinum, and other areas (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: moderate).	ENDORSED
Recommendation 1.5 (Adapted): For patients being considered for maximal surgical cytoreduction, a mediastinoscopy and/or endobronchial US should be considered. (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong). **Justification for modifications to Recommendation 1.5:** As stated in the ASCO guideline, "The proper staging of malignant pleural mesothelioma requires a combination of imaging studies (CT/MRI/PET), lymph node sampling (mediastinoscopy, EBUS, EUS), and surgical exploration to determine the extent of involvement of the pleural space." The Working Group agreed with this statement and recommended that invasive mediastinal staging should be performed on all patients with mesothelioma considered for multimodality therapy, not just patients with enlarged and/or PET-avid mediastinal nodes, as recommended in the ASCO guideline.	ENDORSED with adaptations
Recommendation 1.6: In the presence of contralateral pleural abnormalities detected on initial PET/CT or chest CT scan, a contralateral thoracoscopy may be performed to exclude contralateral disease (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: moderate).	ENDORSED
Recommendation 1.7: In patients with suspicious findings for intra-abdominal disease on imaging and no other contraindications to surgery, it is strongly recommended that a laparoscopy be performed (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	ENDORSED
Recommendation 2.1: The current AJCC/UICC staging classification remains difficult to apply to clinical staging with respect to both T and N components and thus may be imprecise in predicting prognosis. Physicians should recognize that in patients with clinical stage I/II disease, upstaging may occur at surgery (Type of recommendation: evidence based; Evidence quality: high; Strength of recommendation: strong).	ENDORSED

Table 1-2. Recommendations of the American Society of Clinical Oncology guidelines for the treatment of malignant pleural mesothelioma: Staging	
Recommendation	**Assessment**
Recommendation 3.1: The optimal approach to mesothelioma measurement requires the expertise of a radiologist to identify measurement sites on CT as per modified RECIST for mesothelioma. This approach requires calculating the sum of up to six measurement sites with at least 1 cm thickness, measured perpendicular to the chest wall or mediastinum, with no more than two sites on each of three CT sections, separated by at least 1 cm axially (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong). **Implementation Considerations for Recommendation 3.1:** This is the optimal approach, but it may not always be practical to follow.	ENDORSED with implementation considerations
Recommendation 3.2: Assessment of tumour volume by CT scan may enhance clinical staging and provide prognostic information but remains investigational and thus is not recommended (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	ENDORSED
Recommendation 3.3: It is recommended that tumour response classification be determined based on RECIST criteria from the comparisons of these sums across serial CT scans (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong). **Implementation Considerations for Recommendation 3.3:** This is the optimal approach, but it may not always be practical to follow.	ENDORSED with implementation considerations

Abbreviations: AJCC, American Joint Committee on Cancer; ASCO, American Society of Clinical Oncology; CCO, Cancer Care Ontario; CT, computed tomography; EBUS, endobronchial ultrasound; EUS, endoscopic ultrasound; FDG, fluorodeoxyglucose; IV, intravenous; MRI, magnetic resonance imaging; PET, positron emission tomography; RECIST, Response Evaluation Criteria In Solid Tumors; UICC, Union for International Cancer Control; US, ultrasound

Table 1-3. Recommendations of the American Society of Clinical Oncology guidelines for the treatment of malignant pleural mesothelioma: Chemotherapy	
Recommendation	**Assessment**
Recommendation 1.1: Chemotherapy should be offered to patients with mesothelioma because it improves survival and quality of life (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	ENDORSED
Recommendation 1.2: In asymptomatic patients with epithelial histology and minimal pleural disease who are not surgical candidates, a trial of close observation may be offered prior to the initiation of chemotherapy (Type of recommendation: informal consensus; Strength of recommendation: moderate).	ENDORSED
Recommendation 1.3: Selected patients with a poor performance status (PS 2) may be offered single-agent chemotherapy or palliative care alone. Patients with a PS of 3 or greater should receive palliative care (Type of recommendation: evidence based; Evidence quality: low; Strength of recommendation: moderate). **Implementation Considerations for Recommendation 1.3:** Single-agent pemetrexed is not funded for this indication in Ontario.	ENDORSED with implementation considerations
Recommendation 2.1: The recommended first-line chemotherapy for patients with mesothelioma is an antifolate (either pemetrexed or raltitrexed) plus platinum. However, patients should also be offered the option of enrolling in a clinical trial (Type of recommendation: evidence based; Evidence quality: high; Strength of recommendation: strong). **Justification for modifications to Recommendation 2.1:** The Working Group decided to add raltitrexed to the recommendation because, as stated in the ASCO systematic review, raltitrexed demonstrated similar beneficial effects in overall survival and response rates to pemetrexed compared with cisplatin alone [1].	ENDORSED with adaptations

Table 1-3. Recommendations of the American Society of Clinical Oncology guidelines for the treatment of malignant pleural mesothelioma: Chemotherapy	
Recommendation	**Assessment**
Recommendation 3.1: The addition of bevacizumab to pemetrexed-based chemotherapy improves survival in select patients and therefore may be offered to patients with no contraindications to bevacizumab. The randomized clinical trial demonstrating benefit with bevacizumab used cisplatin/pemetrexed; data with carboplatin/pemetrexed plus bevacizumab are insufficient for a clear recommendation (Type of recommendation: evidence based; Evidence quality: high; Strength of recommendation: moderate). **Implementation Considerations for Recommendation 3.1:** Bevacizumab is not funded for this indication in Ontario.	ENDORSED with implementation considerations
Recommendation 3.2: Bevacizumab is not recommended for patients with PS 2, substantial cardiovascular comorbidity, uncontrolled hypertension, age >75, bleeding or clotting risk, or other contraindications to bevacizumab (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: moderate).	ENDORSED
Recommendation 4.0: In patients who may not be able to tolerate cisplatin, carboplatin may be offered as a substitute for cisplatin (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	ENDORSED
Recommendation 5.1: Retreatment with pemetrexed-based chemotherapy may be offered in pleural mesothelioma patients who achieved durable (>6 months) disease control with first-line pemetrexed-based chemotherapy (Type of recommendation: evidence based; Evidence quality: low; Strength of recommendation: moderate). **Implementation Considerations for Recommendation 5.1**: There is a potential gap in funding. Pemetrexed as second-line therapy may not be funded in Ontario.	ENDORSED with implementation considerations
Recommendation 5.2: Given the very limited activity of second-line chemotherapy in patients with mesothelioma, participation in clinical trials is recommended (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	ENDORSED
Recommendation 5.3: In patients for whom clinical trials are not an option, vinorelbine may be offered as second-line therapy (Type of recommendation: evidence based; Evidence quality: low; Strength of recommendation: moderate). **Implementation Considerations for Recommendation 5.3:** Vinorelbine is not funded as second-line therapy in Ontario.	ENDORSED with implementation considerations
Recommendation 6.1: In select asymptomatic patients with epithelial mesothelioma and a low disease burden who are not surgical candidates, a trial of expectant observation, with close monitoring, may be offered before initiation of systemic therapy (Type of recommendation: evidence based; Evidence quality: low; Strength of recommendation: moderate). **Implementation Considerations for Recommendation 6.1:** This is not a common strategy for these patients.	ENDORSED with implementation considerations
Recommendation 6.2: Front-line pemetrexed-based chemotherapy should be given for four to six cycles. For patients with stable or responding disease, a break from chemotherapy is recommended at that point (Type of recommendation: evidence based; Evidence quality: low; Strength of recommendation: moderate).	ENDORSED
Recommendation 6.3: There is insufficient evidence to support the use of maintenance chemotherapy and thus it is not recommended (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	ENDORSED
Recommendation 6.4: There is insufficient evidence to support the use of pemetrexed maintenance in mesothelioma patients and thus it is not recommended (Type of recommendation: evidence based; Evidence quality: low; Strength of recommendation: strong).	ENDORSED

Table 1-4. Recommendations of the American Society of Clinical Oncology guidelines for the treatment of malignant pleural mesothelioma: Surgical cytoreduction	
Recommendation	**Assessment**
Recommendation 1.1 (Adapted): In selected patients with early-stage disease, it is recommended that a maximal surgical cytoreduction should be performed in an expert centre (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: moderate). **Justification for modifications to Recommendation 1.2:** Since the evidence quality was intermediate for this recommendation, the Working Group believed the strength of this recommendation should be moderate instead of strong. The Working Group also agreed that surgical cytoreduction should be performed in an expert centre.	ENDORSED with adaptations
Recommendation 1.2 (Adapted): Maximal surgical cytoreduction as a single modality treatment is generally insufficient; additional antineoplastic treatment (chemotherapy and/or radiation therapy) should be administered. It is recommended that this treatment decision should be made with multidisciplinary input involving thoracic surgeons with an expertise in extrapleural pneumonectomy or lung-sparing cytoreduction (P/D, extended P/D), pulmonologists, medical and radiation oncologists, and radiologists (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong). **Justification for modifications to Recommendation 1.2:** The Working Group believed that thoracic surgeons with an expertise in this type of surgery should be involved in the assessment. Radiologists were added to the multidisciplinary input because they can help decide whether mesothelioma is at an early stage.	ENDORSED with adaptations
Recommendation 1.3 (Adapted): This recommendation has been removed. **Justification for modifications to Recommendation 1.3:** The original ASCO recommendation was 'Patients with transdiaphragmatic disease, multifocal chest wall invasion, or histologically confirmed contralateral mediastinal or supraclavicular lymph node involvement should undergo neoadjuvant treatment before consideration of maximal surgical cytoreduction. Contralateral (N3) or supraclavicular (N3) disease should be a contraindication to maximal surgical cytoreduction." The Working Group believed it is rare for this subset of patients to undergo surgery. As stated in the ASCO guideline, "Diffuse chest wall or transdiaphragmatic involvement represent T4 disease, classically characteristic of a locally advanced, technically unresectable tumor." Also, "For patients with N2 disease, the brief median survival and the absence of long-term survivors mandates against an initial surgical approach." Therefore, these patients would normally not be considered for surgery.	REMOVED
Recommendation 2.1: Patients with histologically confirmed sarcomatoid mesothelioma should not be offered maximal surgical cytoreduction (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	ENDORSED
Recommendation 2.2: Patients with ipsilateral histologically confirmed mediastinal lymph node involvement should only undergo maximal surgical cytoreduction in the context of multimodality therapy (neoadjuvant or adjuvant chemotherapy). Optimally, these patients should be enrolled in clinical trials. (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	ENDORSED

Table 1-4. Recommendations of the American Society of Clinical Oncology guidelines for the treatment of malignant pleural mesothelioma: Surgical cytoreduction	
Recommendation	**Assessment**
Recommendation 3.0 (Adapted): Maximal surgical cytoreduction involves either EPP or lung-sparing options (P/D, extended P/D) and may be offered in highly selected patients when performed in centres of excellence. (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong). **Justification for modifications to Recommendation 3.0:** The original ASCO recommendation recommended lung-sparing surgery over EPP. However, there is no definitive evidence to recommend lung-sparing options over EPP. The very low quality of this evidence is also stated in the ASCO guideline, "Since disease volume is a recognized prognostic factor in malignant pleural mesothelioma, this may confound interpretation of surgical comparisons. Unfortunately, no studies that compare outcomes from EPP and P/D measured disease volume. Such a study would be able to quantitatively compare the operations in patients with similar disease volumes to see if a lung-sparing approach is equivalent or even superior at a given pathologic stage."	ENDORSED with adaptations
Recommendation 4.1.1: A maximal cytoreduction (either lung sparing or non-lung sparing) should only be considered in patients who meet specific preoperative cardiopulmonary functional criteria, have no evidence of extrathoracic disease, and are able to receive multimodality treatment (adjuvant or neoadjuvant) (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	ENDORSED
Recommendation 4.1.2: In patients who have a symptomatic pleural effusion, who are PS 2 or greater, or in whom a maximal cytoreduction cannot be performed (due to disease extent or comorbid conditions), palliative approaches such as a tunneled permanent catheter placement or thoracoscopic exploration with partial resection and/or pleurodesis should be offered. In the latter case, additional biopsy to confirm pathologic diagnosis should be performed during the procedure. If the patient is being evaluated for investigational therapy, material for additional studies (eg, molecular and/ or immunologic profiling) should be obtained. (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	ENDORSED
Recommendation 4.2: In patients who have a symptomatic pericardial effusion, percutaneous catheter drainage or pericardial window may be performed (Type of recommendation: evidence based; Evidence quality: high; Strength of recommendation: strong).	ENDORSED
Recommendation 5.1: Since surgical cytoreduction is not expected to yield an R0 resection, it is strongly recommended that multimodality therapy with chemotherapy and/or radiation therapy should be administered (Type of recommendation: evidence-based; Evidence quality: intermediate; Strength of recommendation: strong).	ENDORSED
Recommendation 5.2: Chemotherapy may be given pre- or postoperatively in the context of multimodality treatment (Type of recommendation: evidence based; Evidence quality: low; Strength of recommendation: moderate).	ENDORSED
Recommendation 5.3: Adjuvant radiation therapy may be associated with a decreased risk of local recurrence and may be offered to patients who have undergone maximal cytoreduction. Treatment is complex, and it is recommended that it should be delivered at experienced centres of excellence (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: moderate).	ENDORSED
Recommendation 5.4: In the context of multimodality treatment, four to six cycles of pemetrexed/platin-based chemotherapy may be administered pre- or postoperatively (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: moderate).	ENDORSED
Recommendation 6.0: Intracavitary therapies (chemotherapy or photodynamic therapy) may be administered safely in experienced centres of excellence, preferably in the context of a clinical trial. Their role in improving outcome is indeterminate (Type of	ENDORSED

Table 1-4. Recommendations of the American Society of Clinical Oncology guidelines for the treatment of malignant pleural mesothelioma: Surgical cytoreduction	
Recommendation	**Assessment**
recommendation: evidence based; Evidence quality: low; Strength of recommendation: weak).	
Recommendation 7.1: Tunneled pleural catheters are not recommended in patients who are candidates for maximal surgical cytoreduction, because of the risk of tumour implantation into the chest wall (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	ENDORSED
Recommendation 7.2: In patients who are not candidates for maximal surgical cytoreduction, tunneled pleural catheters or pleurodesis (performed via chest tube or thoracoscopy) may be offered. As noted above, these procedures should be performed using the minimal number and size incisions. Multidisciplinary input including surgical consultation with a centre of excellence should be sought to optimize management of a pleural effusion and for consideration of investigational intracavitary therapies (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	ENDORSED

Abbreviations: ASCO, American Society of Clinical Oncology; EPP, extrapleural pneumonectomy; P/D, pleurectomy with decortication

Table 1-5. Recommendations of the American Society of Clinical Oncology guidelines for the treatment of malignant pleural mesothelioma: Radiation therapy	
Recommendation	**Assessment**
Recommendation 1.1: Prophylactic irradiation of intervention tracts should generally not be offered patients to prevent tract recurrences (Type of recommendation: evidence based; Evidence quality: high; Strength of recommendation: moderate).	ENDORSED
Recommendation 1.2: It is recommended that adjuvant radiation should be offered to patients who have resection of intervention tracts found to be histologically positive (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: moderate).	ENDORSED
Recommendation 2.1: Radiation therapy should be offered as an effective treatment modality to palliate patients with symptomatic disease (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	ENDORSED
Recommendation 2.2: It is recommended that standard dosing regimens used in other diseases be offered to patients with mesothelioma (8 Gy × one fraction, 4 Gy × five fractions, or 3 Gy × 10 fractions) (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	ENDORSED
Recommendation 3.0: Radiation therapy may be offered to patients with localized asymptomatic recurrence. The dosing fractionation is dependent on the site and extent of disease and should be determined by the radiation oncologist in consultation with the patient (Type of recommendation: informal consensus; Strength of recommendation: moderate).	ENDORSED
Recommendation 4.1: Hemithoracic adjuvant radiation therapy may be offered to patients who undergo non–lung-sparing cytoreductive surgery (EPP), preferably in centres of excellence with experience in this modality for mesothelioma (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	ENDORSED
Recommendation 4.2: Hemithoracic neo-adjuvant radiation therapy may be offered to patients who undergo non–lung-sparing cytoreductive surgery. This potentially toxic regimen remains experimental and should only be performed in highly experienced	ENDORSED

Table 1-5. Recommendations of the American Society of Clinical Oncology guidelines for the treatment of malignant pleural mesothelioma: Radiation therapy	
Recommendation	**Assessment**
centres within the context of a clinical trial (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: moderate).	
Recommendation 5.1: Hemithoracic adjuvant intensity-modulated radiation therapy may be offered to patients who undergo lung-sparing cytoreductive surgery (P/D or EPD). This potentially toxic regimen should only be performed in highly experienced centres, preferably in the context of a clinical trial (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: moderate).	ENDORSED
Recommendation 5.2 (Adapted): Due to the potential for severe pulmonary toxicity, neoadjuvant hemithoracic radiation therapy is not recommended for patients who undergo lung-sparing surgical cytoreductive surgery, except under the context of a clinical trial. **Justification for modifications to Recommendation 5.2:** The word hemithoracic was added for clarity since this type of radiation therapy demonstrated severe pulmonary toxicity as mentioned in the ASCO guideline.	ENDORSED with adaptations
Recommendation 6.1: For palliative radiation therapy, electrons, 2D, 3D, and IMRT may be considered appropriate techniques depending on location of the treatment target and organs at risk (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	ENDORSED
Recommendation 6.2: For adjuvant or neoadjuvant hemithoracic radiation therapy, 3D or IMRT may be offered, respecting guidelines of organs at risk. Proton therapy may be considered in centres with significant experience, preferably in the context of a clinical trial (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	ENDORSED
Recommendation 7.0: It is recommended that standard dosimetric guidelines for organs at risk be used as established predictors of radiation toxicity (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong). **Implementation Considerations for Recommendation 7.0:** The dosimetric constraints should be more restrictive with lung-sparing versus non-lung sparing surgery. As mentioned in the ASCO guideline, there is an association of mean lung dose and the volume of lung receiving 10 Gy with the development of pneumonitis [2].	ENDORSED with implementation considerations

Abbreviations: 2D, two-dimensional; 3D, three-dimensional; ASCO, American Society of Clinical Oncology; EPD, extended pleurectomy with decortication; EPP, extrapleural pneumonectomy; IMRT, intensity-modulated radiation therapy; P/D, pleurectomy with decortication

Endorsement of the 2018 American Society of Clinical Oncology Treatment of Malignant Pleural Mesothelioma Guideline

Section 2: Endorsement Methods Overview

THE PROGRAM IN EVIDENCE-BASED CARE

The Program in Evidence-Based Care (PEBC) is an initiative of the Ontario provincial cancer system, Cancer Care Ontario (CCO). The PEBC's mandate is to improve the lives of Ontarians affected by cancer through the development, dissemination, and evaluation of evidence-based products designed to facilitate clinical, planning, and policy decisions about cancer control.

The PEBC is a provincial initiative of CCO supported by the Ontario Ministry of Health and Long-Term Care (OMHLTC). All work produced by the PEBC is editorially independent from the OMHLTC.

BACKGROUND FOR GUIDELINE

There were originally three guidelines, divided into chemotherapy, surgical, and radiation therapy topics, that covered the treatment of patients with malignant pleural mesothelioma. The CCO Lung Cancer Disease Site Group (DSG) decided to update the evidence for the treatment of malignant pleural mesothelioma and create one guideline covering systemic therapy, radiation therapy, and surgery. They believed that some of the recommendations, especially with regard to radical radiation treatment, may change with a review of newer evidence.

GUIDELINE ENDORSEMENT DEVELOPERS

This endorsement was developed by the Treatment of Malignant Pleural Mesothelioma GDG (Appendix 1), which was convened at the request of the Lung Cancer DSG. The project was led by a small Working Group of the Treatment of Malignant Pleural Mesothelioma GDG, which was responsible for reviewing the evidence base and recommendations in detail and making an initial determination as to any necessary changes, drafting the first version of the endorsement document, and responding to comments received during the document review process. The Working Group members had expertise in medical oncology, radiation oncology, surgical oncology, radiology, pathology, and health research methodology. Other members of the Treatment of Malignant Pleural Mesothelioma GDG served as the Expert Panel and were responsible for the review and approval of the draft document produced by the Working Group. Conflict of interest declarations for all GDG members are summarized in Appendix 1, and were managed in accordance with the *PEBC Conflict of Interest Policy*.

ENDORSEMENT METHODS

The PEBC endorses or adapts guidelines using the methods of CCO's Guideline Endorsement Protocol [3]. This process includes assessment of the recommendations and drafting an endorsement document by the Working Group, internal review by content and methodology experts, and external review by Ontario clinicians and other stakeholders. Implementation considerations such as costs, human resources, and unique requirements for special or disadvantaged populations may be provided along with the recommendations for information purposes.

The PEBC assesses the quality of guidelines using the AGREE II tool [4]. AGREE II is a 23-item validated tool that is designed to assess the methodological rigour and transparency of guideline development [4].

Selection of Guidelines

As a first step in developing this document, a search for existing guidelines was undertaken to determine whether any guideline could be adapted or endorsed. Evidence-based guidelines with systematic reviews that addressed the research question, 'Which treatment strategy leads to the greatest benefit and least adverse effects for patients with malignant pleural mesothelioma', were included. Guidelines older than three years (published before 2014) were excluded. Guidelines based on consensus or expert opinion were excluded. The following sources were searched for existing guidelines on November 16, 2017 with the search term mesothelioma: National Guideline Clearing House, National Institute for Health and Care Excellence Evidence Search, Canadian Medical Association Journal Infobase, Scottish Intercollegiate Guidelines Network, American Association of Clinical Oncology, National Health and Medical Research Council – Australia Clinical Practice Guidelines Portal, and Cancer Council Australia – Cancer Guidelines Wiki. One guideline developed by ASCO met the inclusion criteria [1].

Assessment of the ASCO Guideline

The quality of the ASCO guideline [1] was assessed using the AGREE II tool [4] (see Table 2-1). The Working Group considered the guideline to be of high quality because the rigour of development domain, which assesses the methodological quality of the guideline, was well above 50% (Table 2-1).

Table 2-1. Results of AGREE II Tool quality rating of the evidence-based guideline.

Guideline	AGREE II Domain Scores					
	Scope and Purpose (%)	Stakeholder Involvement (%)	Rigour of Development (%)	Clarity and Presentation (%)	Applicability (%)	Editorial Independence (%)
ASCO 2018 [1]	100	76	90	100	70	89

Abbreviations: ASCO, American Society of Clinical Oncology

DESCRIPTION OF ASCO'S GUIDELINE

The ASCO guideline covered five topics: diagnosis, staging, chemotherapy, surgical cytoreduction, and radiation therapy [1]. Recommendations were generated by their Expert Panel based on randomized controlled trials, prospective and retrospective observational studies, and their clinical experience. Their guideline was circulated to external reviewers and approved by their Expert Panel and the ASCO Clinical Practice Guideline Committee.

ENDORSEMENT PROCESS

During two teleconferences, the Working Group reviewed each of the recommendations from ASCO to assess whether they agreed with the interpretation of the evidence and the justification of each recommendation. They assessed the applicability of each recommendation in Ontario and whether additional clarification would be needed. They also assessed whether new evidence reported since the guideline was developed might change any of the recommendations.

The Working Group endorsed most of the recommendations from ASCO, which have been reprinted here with permission for any modifications [1].[2] Modifications to six of ASCO's recommendations were based on differences in the interpretation of the evidence and one recommendation was removed. The rationales for these changes are listed in Table 2-2 and can also be found in Section 1. Recommendations that were endorsed with no modifications do not appear in Table 2-2. For the endorsed recommendations without modifications, the Working Group agreed with ASCO's justifications and the reader is referred to the ASCO guideline for their justification [1].

[2]

Table 2-2 Modifications to the ASCO recommendations

ASCO recommendations	Modifications	Modification rationale	Implementation considerations
STAGING Recommendation 1.2. An FDG PET/CT should usually be obtained for initial staging of patients with mesothelioma. This may be omitted in patients who are not being considered for definitive surgical resection (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	No modifications		This may need to be reconsidered by the PET program at CCO as to whether it should be added to the list of approved indications.
STAGING Recommendation 1.5. For patients being considered for maximal surgical cytoreduction, a mediastinoscopy and/or endobronchial US should be considered if enlarged and/or PET-avid mediastinal nodes are present (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	Rewrite as, "For patients being considered for maximal surgical cytoreduction, a mediastinoscopy and/or endobronchial US should be considered."	As stated in the ASCO guideline, "The proper staging of malignant pleural mesothelioma requires a combination of imaging studies (CT/MRI/PET), lymph node sampling (mediastinoscopy, EBUS, EUS), and surgical exploration to determine the extent of involvement of the pleural space." Therefore, invasive mediastinal staging should be performed on all patients with mesothelioma considered for multimodality therapy.	
STAGING Recommendation 3.1. The optimal approach to mesothelioma measurement requires the expertise of a radiologist to identify measurement sites on CT as per modified RECIST for mesothelioma. This approach requires calculating the sum of up to six measurement sites with at least 1 cm thickness, measured perpendicular to the chest wall or mediastinum, with no more than two sites on each of three CT sections, separated by at least 1 cm axially (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	No modifications		This is the optimal approach, but it may not always be practical to follow.
STAGING Recommendation 3.3. It is recommended that tumour response classification be determined	No modifications		This is the optimal

based on RECIST criteria from the comparisons of these sums across serial CT scans (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).			approach, but it may not always be practical to follow.
CHEMOTHERAPY Recommendation 1.3. Selected patients with a poor performance status (PS 2) may be offered single-agent chemotherapy or palliative care alone. Patients with a PS of 3 or greater should receive palliative care (Type of recommendation: evidence based; Evidence quality: low; Strength of recommendation: moderate).	No modifications		Single-agent pemetrexed is not funded for this indication in Ontario.
CHEMOTHERAPY Recommendation 2.1. The recommended first-line chemotherapy for patients with mesothelioma is pemetrexed plus platinum. However, patients should also be offered the option of enrolling in a clinical trial (Type of recommendation: evidence based; Evidence quality: high; Strength of recommendation: strong).	Added raltitrexed to the recommendation	The Working Group decided to add raltitrexed to the recommendation because, as stated in the ASCO systematic review, raltitrexed demonstrated similar beneficial effects in overall survival and response rates to pemetrexed compared with cisplatin alone.	
CHEMOTHERAPY Recommendation 3.1. The addition of bevacizumab to pemetrexed-based chemotherapy improves survival in select patients and therefore may be offered to patients with no contraindications to bevacizumab. The randomized clinical trial demonstrating benefit with bevacizumab used cisplatin/pemetrexed; data with carboplatin/ pemetrexed plus bevacizumab are insufficient for a clear recommendation (Type of recommendation: evidence based; Evidence quality: high; Strength of recommendation: moderate).	No modifications		Bevacizumab is not funded for this indication in Ontario.
CHEMOTHERAPY Recommendation 5.1. Retreatment with pemetrexed-based chemotherapy may be offered in pleural mesothelioma patients who achieved durable (>6 months) disease control with first-line pemetrexed-based chemotherapy (Type of recommendation: evidence based; Evidence	No modifications		There is a potential gap in funding. Pemetrexed as second-line therapy may not

quality: low; Strength of recommendation: moderate).			be funded in Ontario.
CHEMOTHERAPY Recommendation 5.3. In patients for whom clinical trials are not an option, vinorelbine may be offered as second-line therapy (Type of recommendation: evidence based; Evidence quality: low; Strength of recommendation: moderate).	No modifications		Vinorelbine is not funded as second-line therapy in Ontario.
CHEMOTHERAPY Recommendation 6.1. In select asymptomatic patients with epithelial mesothelioma and a low disease burden who are not surgical candidates, a trial of expectant observation, with close monitoring, may be offered before initiation of systemic therapy (Type of recommendation: evidence based; Evidence quality: low; Strength of recommendation: moderate).	No modifications		This is not a common strategy for these patients.
SURGICAL CYTOREDUCTION Recommendation 1.1. In selected patients with early-stage disease, it is strongly recommended that a maximal surgical cytoreduction should be performed (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	We removed 'strongly' from this recommendation and changed the strength of the recommendation to moderate. We added that surgical cytoreduction should be performed in an expert centre.	Since the evidence quality was intermediate for this recommendation, the Working Group believed the strength of this recommendation should be moderate instead of strong. The Working Group also agreed that surgical cytoreduction should be performed in an expert centre.	
SURGICAL CYTOREDUCTION Recommendation 1.2. Maximal surgical cytoreduction as a single modality treatment is generally insufficient; additional antineoplastic treatment (chemotherapy and/or radiation therapy) should be administered. It is recommended that this treatment decision should be made with multidisciplinary input involving thoracic surgeons, pulmonologists, medical and radiation	Specify that thoracic surgeons should have expertise with this type of surgery. Also, include radiologists in the	The Working Group believed that thoracic surgeons with an expertise in this type of surgery should be involved in the assessment. Radiologists can help decide whether mesothelioma is at an early stage.	

oncologists (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	multidisciplinary input.		
SURGICAL CYTOREDUCTION Recommendation 1.3. Patients with transdiaphragmatic disease, multifocal chest wall invasion, or histologically confirmed contralateral mediastinal or supraclavicular lymph node involvement should undergo neoadjuvant treatment before consideration of maximal surgical cytoreduction. Contralateral (N3) or supraclavicular (N3) disease should be a contraindication to maximal surgical cytoreduction (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	This recommendation has been removed.	It is rare for this subset of patients to undergo surgery. As stated in the ASCO guideline, "Diffuse chest wall or transdiaphragmatic involvement represent T4 disease, classically characteristic of a locally advanced, technically unresectable tumor." Also, "For patients with N2 disease, the brief median survival and the absence of long-term survivors mandates against an initial surgical approach." Therefore, these patients would normally not be considered for surgery.	
SURGICAL CYTOREDUCTION Recommendation 3.0. Maximal surgical cytoreduction involves either EPP or lung-sparing options (P/D, extended P/D). When offering maximal surgical cytoreduction, lung-sparing options should be the first choice, due to decreased operative and long-term risk. EPP may be offered in highly selected patients when performed in centres of excellence (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	Maximal surgical cytoreduction involves either EPP or lung-sparing options (P/D, extended P/D) and may be offered in highly selected patients when performed in centres of excellence.	There is no definitive evidence to recommend lung-sparing options over EPP. The very low quality of this evidence is also stated in the ASCO guideline, "Since disease volume is a recognized prognostic factor in malignant pleural mesothelioma, this may confound interpretation of surgical comparisons. Unfortunately, no studies that compare outcomes from EPP and P/D measured disease volume. Such a study would be able to quantitatively compare the operations in patients with similar disease volumes to see if a lung-sparing approach is equivalent or even superior at a given pathologic stage."	
RADIATION THERAPY Recommendation 5.2. Due to the potential for severe pulmonary toxicity, neoadjuvant radiation therapy is not recommended for patients who undergo lung-sparing surgical cytoreductive surgery (Type of recommendation: informal consensus; Strength of recommendation: strong).	Due to the potential for severe pulmonary toxicity, neoadjuvant hemithoracic radiation therapy is not recommended for patients who undergo lung-	The word hemithoracic was added for clarity since this type of radiation therapy demonstrated severe pulmonary toxicity as mentioned in the ASCO guideline.	

	sparing surgical cytoreductive surgery, except under the context of a clinical trial.		
RADIATION THERAPY Recommendation 7.0. It is recommended that standard dosimetric guidelines for organs at risk be used as established predictors of radiation toxicity (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).	No modifications		The dosimetric constraints should be more restrictive with lung-sparing versus non-lung sparing surgery. As mentioned in the ASCO guideline, there is an association of mean lung dose and the volume of lung receiving 10 Gy with the development of pneumonitis [2]

Abbreviations: ASCO, American Society of Clinical Oncology; CCO, Cancer Care Ontario; CT, computed tomography; EBUS, endobronchial ultrasound; EPP, extrapleural pneumonectomy; EUS, endoscopic ultrasound; FDG PET, fluorodeoxyglucose positron emission tomography, Gy, Gray; MRI, magnetic resonance imaging; P/D, pleurectomy with decortications; RECIST, Response Evaluation Criteria In Solid Tumors; US, ultrasound

ENDORSEMENT REVIEW AND APPROVAL

Internal Review

For the endorsement document to be approved, 75% of the content experts who comprise the GDG Expert Panel must cast a vote indicating whether or not they approve the document, or abstain from voting for a specified reason, and of those that vote, 75% must approve the document. In addition, the PEBC Director, with methodology expertise, must approve the document. The Expert Panel and the PEBC Director may specify that approval is conditional, and that changes to the document are required.

External Review

Feedback on the approved draft endorsement document is obtained from content experts through Professional Consultation. Relevant care providers and other potential users of the endorsement document are contacted and asked to provide feedback on the recommendations through a brief online survey. This consultation is intended to facilitate the dissemination of the final guidance report to Ontario practitioners.

UPDATING THE ENDORSEMENT

The Lung Cancer DSG will review this endorsement on an annual basis to ensure that it remains relevant and appropriate for use in Ontario.

ACKNOWLEDGEMENTS

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- Melissa Brouwers and Sheila McNair for providing feedback on draft versions.
- Sara Miller for copy editing.

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Section 3: Internal and External Review

INTERNAL REVIEW

The endorsement was evaluated by the GDG Expert Panel (Appendix 1). The results of these evaluations and the Working Group's responses are described below.

Expert Panel Review and Approval

Of the 24 members of the GDG Expert Panel, 18 members voted and one abstained, for a total of 79% response in August 2018. Of those who voted, 18 approved the document (100%). The main comments from the Expert Panel and the Working Group's responses are summarized in Table 3-1.

Table 3-1. Summary of the Working Group's responses to comments from the Expert Panel.

Comments	Responses
1. For Recommendation 1.1 under surgical cytoreduction, I do not think we can make a strong recommendation for cytoreduction surgery when the evidence is conflicting and weak at best.	We removed 'strongly' from this recommendation and changed the strength of the recommendation to moderate.
2. Clarify that recommendation 3.0 under "radiation therapy" relates to patients who underwent maximal cytoreductive surgery?	The Working Group decided not to change this recommendation because they may offer radiation therapy to patients with small asymptomatic mesothelioma recurrences with stereotactic body radiation therapy who did not undergo maximal cytoreductive surgery.

EXTERNAL REVIEW

Professional Consultation

Feedback was obtained through a brief online survey of healthcare professionals and other stakeholders who are the intended users of the endorsement document. All professionals with an interest in lung cancer in the PEBC database, members of the Canadian Mesothelioma Association, and members of the International Mesothelioma Interest Group were contacted by email to inform them of the survey. One hundred twenty-three professionals were contacted, of whom 100 practiced in Ontario. Twenty-two (18%) responses were received. Eight people stated that they did not have interest in this area or were unavailable to review this endorsement document at the time. The results of the feedback survey from 14 people are summarized in Table 3-2. The main comments from the consultation and the Working Group's responses are summarized in Table 3-3.

Table 3-2. Responses to four items on the professional consultation survey.

	Number (%)				
General Questions: Overall Guideline Assessment	Lowest Quality (1)	(2)	(3)	(4)	Highest Quality (5)
1. Rate the overall quality of the guideline report.	0	0	0	7 (50)	7 (50)
	Strongly Disagree (1)	(2)	(3)	(4)	Strongly Agree (5)
2. I would make use of this guideline in my professional decisions.	0	0	0	7 (50)	7 (50)
3. I would recommend this guideline for use in practice.	0	0	0	6 (43)	8 (57)
4. What are the barriers or enablers to the implementation of this guideline report?	• Barriers to implementation include dissemination to the appropriate parties involved in the diagnosis (i.e., respirologists and thoracic surgeons across the province). • In clinical practice, with the exception of clinical trials, RECIST criteria are rarely used to assess response as this is impractical. • Although the guideline makes caveats about funding for certain drugs in Ontario, it still remains a barrier toward implementation locally. • Very few patients are ever considered for maximal cytoreductive surgery and hence there are few "centres of excellence". • These guidelines merit further discussion at the PET Steering Committee for consideration to become insured indications. These patients at this time would be eligible through the PET access program so there is no barrier to provision of this service at this time. That being said, usage, once insured, is usually more consistent and widespread. However, availability of PET scanning for these patients may vary from province to province, centre to centre.				

Table 3-3. Summary of the Working Group's responses to comments from professional consultants.

Comments	Responses
1. In order to improve the message on current standard chemotherapy, include platin and any other antifolate.	We added raltitrexed to recommendation 2.1 under chemotherapy.
2. There was a suggestion to add that cytoreductive surgery should only be performed in expert centres.	We added this to recommendation 1.1 under surgical cytoreduction.
3. It would have been helpful if criteria for selection of patients for surgical resection	The Working Group decided to add "It is recommended that this treatment decision should be

were given in more detail (age, PS, extent of disease etc.).	made with multidisciplinary input involving thoracic surgeons, with an expertise in extrapleural pneumonectomy or lung-sparing cytoreduction (P/D, extended P/D)...” to recommendation 1.2 under surgical cytoreduction because they would be better equipped to assist in the selection of patients for this type of surgery.

CONCLUSION

The final endorsed recommendations contained in Section 1 reflect the integration of feedback obtained through the external review processes with the document as drafted by the GDG Working Group and approved by the GDG Expert Panel.

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Appendix 1: Affiliations and Conflict of Interest Declarations

In accordance with the PEBC Conflict of Interest (COI) Policy, the Members of the Treatment of Malignant Pleural Mesothelioma Working Group, Expert Panel, and the Program in Evidence-Based Care Director were asked to disclose potential conflicts of interest

Name and Affiliation	Declarations of interest
Working Group	
Penelope Bradbury Medical Oncologist Lung Cancer Disease Site Group	Received at least a $5,000 acting in a consulting capacity for AbbVie
John Cho Radiation Oncologist Princess Margaret Cancer Centre, Toronto, Ontario	• Was a principal investigator for the Surgery for Mesothelioma After Radiation Therapy (SMART) study • Published: Cho BC. The rationale for neoadjuvant radiation therapy in malignant pleural mesothelioma: how smart is SMART? Ann Transl Med 2017;5(11):247. doi: 10.21037/atm.2017.04.13 • Published Non-ablative hypofractionated hemithoracic radiation—a new standard of care in mesothelioma? J Thorac Dis 2018. doi: 10.21037/jtd.2018.09.131 • Provided comments to a *Globe and Mail* news article on mesothelioma
Marc de Perrot Thoracic Surgeon Toronto General Hospital Toronto, Ontario	Received honoraria from Bayer for hypertension and from Merck for mesothelioma (not ongoing) for less than $5,000
Carole Dennie Radiologist The Ottawa Hospital Ottawa, Ontario	Spouse received $5,000 or more in a single year as a speaker and in travelling support for Abbott
Peter Ellis Medical Oncologist Lung Cancer Disease Site Group	Received at least a $5,000 honorarium for an advisory role from AbbVie
John Goffin Medical Oncologist Lung Cancer Disease Site Group	• Was a principal investigator for the CCTG Trial involving Pembrolizumab in Mesothelioma • Received an honorarium from Amgen (2014), Boehringer Ingelheim (2015), and Bristol-Myers Squibb (2015) • Received conference travel support from AstraZeneca (2017) • Received a speaking fee from Amgen (2018).
Robert MacRae Radiation Oncologist Lung Cancer Disease Site Group	None declared

Donna Maziak Surgeon Lung Cancer Disease Site Group	None declared
Ming Tsao Pathologist Princess Margaret Cancer Centre Toronto, Ontario	None declared
Yee Ung Radiation Oncologist Lung Cancer Disease Site Group	None declared
Emily Vella Health Research Methodologist Program in Evidence-Based Care	None declared
Lung Cancer Disease Site Group Expert Panel	
Adrien Chan Medical Oncologist Lung Cancer Disease Site Group	None declared
Susanna Cheng Medical Oncologist Lung Cancer Disease Site Group	None declared
Ronald Feld Medical Oncologist Lung Cancer Disease Site Group	Employed by the University Health Network. Retired in June 2017.
Richard Gregg Medical Oncologist Lung Cancer Disease Site Group	None declared
Swati Kulkarni Medical Oncologist Lung Cancer Disease Site Group	None declared
Sara Kuruvilla Medical Oncologist Lung Cancer Disease Site Group	None declared
Scott Laurie Medical Oncologist Lung Cancer Disease Site Group	None declared
Natasha Leighl Medical Oncologist Lung Cancer Disease Site Group	• Merke Sharpe Dohme 2017 over $5,000 for Continuing Medical Education accredited lectures for the Taiwan Pathology Society September 2017 • Received research support from Novartis in 2015 to the University Health Network as a grant for an investigator-initiated trial and from Roche in 2013 to the University Health Network to support correlative studies for an investigator-initiated trial • Clinical expert for pan-Canadian Oncology Drug Review for osimertinib, dabrafenib, trametinib, alectinib 2L, alectinib 1L

Andrew Robinson Medical Oncologist Lung Cancer Disease Site Group	None declared
Mark Vincent Medical Oncologist Lung Cancer Disease Site Group	• Received $5,000 or more in a single year in a consulting capacity from Roche and Eli Lilly • Received a grant from Roche for decision support
Medhat El-Mallah Radiation Oncologist Lung Cancer Disease Site Group	None declared
Conrad Falkson Radiation Oncologist Lung Cancer Disease Site Group	Published opinions on the treatment for malignant pleural mesothelioma Ung YC, Yu E, Falkson C, Haynes AE, Stys-Norman D, Evans WK. Lung Cancer Disease Site Group of Cancer Care Ontario's Program in Evidence-based Care. The role of radiation therapy in malignant pleural mesothelioma: a systematic review. Radiother Oncol. 2006 Jul;80(1):13-8. Epub 2006 Jul 3. Review. Ung Y, Yu E, Falkson CB, and the members of the Lung Disease Site Group. The Role of Radiation Therapy in Malignant Pleural Mesothelioma. Evidence-based Series #7-14 Original Version: February 2006 Reviewed May 2013 Falkson CB, Robinson AG. Malignant Mesothelioma. Reference Module in Biomedical Sciences, 3-2016 (e-pub), Reference Module in Biomedical Sciences. Elsevier. - First Author (Chapter) Falkson CB, Robinson AG. Malignant Mesothelioma in Biomedical Sciences - Cancer and Endocrine Diseases Online Reference Module in Biomedical Sciences, Elsevier 2014. Falkson CB, Falkson G. Malignant Mesothelioma. In: Encyclopedia of Cancer 2nd Edition, Volume 3, 115-118, 2002. Ed Bertino JR. New York Academic Press.
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Mojgan Taremi Radiation Oncologist Lung Cancer Disease Site Group	None declared

Alexander Sun Radiation Oncologist Lung Cancer Disease Site Group	None declared
Edward Yu Radiation Oncologist Lung Cancer Disease Site Group	None declared
Abdollah Behzadi Surgeon Lung Cancer Disease Site Group	None declared
Donald Jones Surgeon Lung Cancer Disease Site Group	None declared
Richard Malthaner Surgeon Lung Cancer Disease Site Group	None declared
Julius Toth Surgeon Lung Cancer Disease Site Group	None declared
Kazuhiro Yasufuku Surgeon Lung Cancer Disease Site Group	None declared
Robert Zeldin Surgeon Lung Cancer Disease Site Group	Acted as an advisor for Boehringer Ingelheim
Program in Evidence-Based Care Director	
Melissa Brouwers Director Program in Evidence-Based Care, Cancer Care Ontario, Hamilton, ON	None declared