Guidelines for the Management of Malignant Melanoma

Preamble Note:
Management guidelines are intended to assist health care professionals with decisions throughout the spectrum of the cancer experience. Guidelines should never replace specific decisions for individual patients, and do not substitute for the shared decisions between any patient and doctor (or other health professional) which are unique to each circumstance. However, guidelines do provide evidence-based background information, consensus-based recommendations for similar problems, and a context for each individual decision.

Objective:
This guideline is for health professionals in Nova Scotia involved in the management of malignant melanoma who want to know the Nova Scotia approach to melanoma. It represents the consensus of the Melanoma Cancer Site Team, based on knowledge and evidence, and reflects the practice policies of the team. The guideline provides an overview including diagnosis and staging, referral, treatment of the primary and recurrence and follow-up and surveillance. It also reviews the supportive care issues faced by patients with malignant melanoma and recommends practices to address these issues. A simplified discussion with flowcharts summarizes the written contents. The hope is that codifying and standardizing current practice will reduce unnecessary practice variation across the province.

Patients, family members and other non-health professionals are encouraged to review materials written specifically for them. The Canadian Cancer Society’s Information Service (1-888-939-3333 or www.cancer.ca) is one source for this type of information.


Comment on Clinical Research:
An important component of treatment decision-making for any patient is the potential for enrollment in relevant clinical research. The Melanoma Cancer Site Team is committed to advancing patient care through participation in clinical trials and other clinical research projects. At any point in time, there may be a clinical trial opportunity for any component of this guideline. As specific trials or clinical research projects become available, eligible patients may be offered the opportunity to enroll in the relevant trial or research project. Every effort will be made to accommodate patients for clinical trial participation within eligibility requirements. Patients are encouraged to discuss clinical trials opportunities with their cancer specialist. Current clinical trials are listed at www.canadiancancertrials.ca.
Acknowledgements:

This guideline was written by a collaborative effort of the Melanoma Cancer Site Team, and was sponsored by Cancer Care Nova Scotia. For further information on this, or any other Practice Guideline, please contact the CST Co-Chairs, or members of the Guidelines Resource Team, Cancer Care Nova Scotia at (902) 473-4645 or 1-866-599-2267 or info@ccns.nshealth.ca

Sections of this document have been used with permission from Richard G.B.H. Langley. (2013). Skin Cancer: An Overview of Non-melanoma Cancers and Melanoma, edition 3. Halifax, Nova Scotia: Cancer Care Nova Scotia

Guideline Approvals:
• Melanoma Cancer Site Team- Initial date approved - 13/09/2006
• Revision with Community Reviewer Input- November 2013
• Cancer Care Nova Scotia, Chief Medical Director - date approved

Recommended Citation:

May be reprinted with permission from Cancer Care Nova Scotia (1-866-599-2267).
GUIDELINES FOR THE MANAGEMENT OF MALIGNANT MELANOMAS

Contents:

1. Introduction 1
2. Management Algorithms 5
3. Diagnosis 10
4. Pathology and Staging 17
5. Surgical Treatment of Malignant Melanomas 22
6. Treatment of Regional Lymph Nodes 24
7. Adjuvant Therapy for High Risk or Advanced Disease 27
8. Treatment of Local Recurrence 29
9. Treatment for Distant Metastases (Stage IV Melanoma) 32
10. Sub-types Melanoma 34
   10.1 Subungual
   10.2 Plantar
   10.3 Melanoma of the Face and Head 38
11. Melanoma in Pregnancy 38
12. Follow-up Practice Guidelines 40
13. Supportive Care Issues 42
14. Referral Process 50

Appendix I Resection margins 53
Appendix II Lymphatic Mapping/
Sentinel Lymph Node Biopsy (SLNBx) 54
Appendix III Primary Invasive Malignant Melanoma
Surgical Pathology Report template 55
Appendix IV Benign Lesions that May Mimic Skin Cancer 56
<table>
<thead>
<tr>
<th>Appendix V</th>
<th>Basic Skin Cancer Treatment Algorithm</th>
<th>58</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appendix VI</td>
<td>Guideline Development Process</td>
<td>59</td>
</tr>
<tr>
<td>References</td>
<td></td>
<td>65</td>
</tr>
<tr>
<td>Melanoma Site Team Members (2001-2013)</td>
<td></td>
<td>74</td>
</tr>
</tbody>
</table>
1. Introduction

Cutaneous melanoma is an increasingly common malignancy of melanocytes. The increased frequency of melanoma is well documented.1-2

The risk of developing malignant melanoma can be significantly reduced by minimizing exposure to ultraviolet radiation. Radiation from the sun and exposure to sunlamps and sunbeds is known to be a human carcinogen causing cutaneous malignant melanoma and nonmelanocytic skin cancer.3-4

The challenge for clinicians is to detect and excise melanoma in its earliest stage, as primary tumor thickness remains the most critical prognostic indicator in this malignancy. Early diagnosis and surgical excision of in situ or early invasive melanomas is curative in most patients. Despite advances in chemotherapy and immunotherapy, the efficacy of treatment of advanced melanoma remains limited, and the prognosis of metastatic disease remains guarded.

Definition

Melanoma results from the malignant transformation of melanocytes. Embryologically, melanocytes are derived from the neural crest, and produce melanin. During embryonic life precursor cells, known as melanoblasts, migrate to the basal cell layer of the epidermis, and less frequently to the dermis and sebaceous glands.3 Melanoma can arise from melanocytes located in these sites and from altered melanocytes called nevus cells in certain precursor lesions.

Epidemiology

In 2013, the Canadian Cancer Society estimated the age-standardized incidence rate for melanoma in Nova Scotia males (23/100,000) and females (19/100,000) will be the highest in the country. The Canadian rate is 15/100,000 for males and 12/100,000 for females.2

Incidence is higher in Canadian men than women with melanoma the 8th most common cancer diagnosis in men and the 11th most common in women. Canadian men have a 1 in 63 (1.6%) lifetime probability of developing melanoma compared to 1 in 79 Canadian women (1.3%).2 Worldwide, of the 160,000 new cases estimated to have occurred in 2002, women were affected slightly more than men (male-to-female ratio, 0.97:1). Conversely, of the estimated 41,000 worldwide deaths in 2002, more occurred in men than in women (male-to-female ratio 1.2:1).6

The incidence of melanoma is increasing faster than any other malignancy in persons with light-colored skin in all parts of the world. From the early 1990s, the annual percent change in age-standardized incidence rates for melanoma in both males and females in Canada has increased at a statistically significant rate.5 In the United States, the current lifetime risk for developing invasive melanoma has increased 2000% since 1930.4
While melanoma is primarily a malignancy of white individuals, it is important to know that melanoma develops in all races.\textsuperscript{7} American data shows that African Americans develop melanoma approximately one twentieth as frequently as white persons, and the prevalence in Hispanics is approximately one sixth of that in white persons; however, they have higher mortality rates.\textsuperscript{6}

Melanomas diagnosed in African-Americans, Asians and Hispanics are often of a less common sub-type or presentation than that diagnosed in whites:

- Acral Lentiginous Melanoma (ALM) accounts for 50\% of all melanomas in Asians and people with dark skin but is only 5\% of all diagnosed melanoma in the US.\textsuperscript{8}
- Subungal melanoma is a higher proportion of melanomas (15\% to 35\%) in dark-skinned ethnic groups but only 3\% of cases of melanoma in whites.\textsuperscript{68}
- Plantar melanoma is rare in whites accounting for only 2\% to 8\% of melanoma cases. However, it arises on the plantar surface of the foot in 35\% to 90\% of patients diagnosed with melanoma of African-American, Asian, or Hispanic descent.\textsuperscript{71}

The dramatic variation of melanoma incidence across ethnic groups is partly accounted for by variations in skin type, though there are additional genetic (e.g. MC1R variation) and cultural/behavioural determinants (e.g. clothing and sun-seeking practices).\textsuperscript{7}

While the lifetime probability of developing melanoma in the next 10 years is highest in men over the age of 60, melanoma is the second-most common cancer in Canadian females between the ages of 15-29.\textsuperscript{2} Melanoma is the fifth-most common cancer accounting for 6\% of cancers diagnosed in Canadians between the ages of 30-49.\textsuperscript{2} In the US, melanoma is the most common cancer in women aged 25-29 years and is second only to breast cancer in women aged 30-34 years.\textsuperscript{6}

A study of melanoma incidence and mortality in whites in the US between 1969-1999 showed the greatest increase in both incidence and mortality was in men over age 65.\textsuperscript{9} Older individuals are both more likely to acquire and to die from melanoma; thus, elderly persons should be a primary target for secondary melanoma prevention, including early detection and screening. Treatment options in elderly persons may also be limited because of comorbid medical conditions, an inability to tolerate adverse medication effects or toxicity, the increased likelihood of drug interactions, and potential exclusion from clinical trials based on age criteria.\textsuperscript{6}

Survival

The five-year relative survival for melanoma for the period 2006-2008 was 89\%; a slight improvement over the period 1992-1994 where it was 85\%. Relative survival for women (92\%) is better than for men (85\%).

Mortality

The 2013 estimated age–standardized mortality rates for melanoma in Nova Scotia is 4/100,000 men and 2/100,000 women, which compares to the Canadian average of 3/100,000 cases in men and 2/100,000 in women.
**Risk factors**

*UV Exposure*


Ultraviolet (UV) radiation from the sun is classified by the International Agency for Research on Cancer (IARC) as a Group 1 carcinogen and cause of melanoma and other skin cancers\(^\text{10}\). Additionally, radiation from UV emitting tanning devices was reclassified in 2009 to a Group 1 carcinogen by the International Agency for Research on Cancer\(^\text{11}\).

Sun exposure is the main driver of melanoma incidence at the population level, with significant contributions made by total lifetime exposure, an intermittent pattern of intense exposure and exposure in childhood and adolescence (as indicated by the ambient solar UV radiation present where a person lives).\(^\text{7}\) The Canadian Dermatology Association says that approximately 90% of melanomas are associated with severe UV exposure and sunburns over a lifetime.\(^\text{12}\)

People who work, play or exercise in the sun for long periods of time are at greater risk\(^\text{13}\). The potential of high UV exposure is greatest in three particular groups: older children and young adults are the most active tanners and they are the least compliant with sun protection practices; outdoor workers are highly exposed to natural UV\(^\text{13}\).

Since most skin cancers are related to over-exposure to the sun, reduction of sun exposure has the potential to substantially reduce the number of cancers. The Canadian Cancer Society estimates that the impact of reduction of sun exposure on the number of new skin cancers prevented would be analogous to the effect of tobacco control on the incidence of lung cancer.\(^\text{5}\)

A study in Cancer, Epidemiology, Biomarkers and Prevention clearly demonstrated an increased melanoma risk in indoor tanners and even more alarming, an escalating risk with total hours, sessions or years of tanning bed use.\(^\text{14}\) The Nova Scotia Tanning Beds Act\(^\text{15}\), proclaimed on May 31, 2011, makes it illegal for people under 19 years of age to use tanning beds.

Health professionals working in primary care should counsel their patients on sun safe practices and to avoid artificial tanning. A recent study found that long-term, regular use of sunscreen significantly reduced the rate of melanoma in adults.\(^\text{16}\)

**Other Risk Factors**

In addition to UV exposure, the development of melanoma is multifactorial and appears to be related to multiple risk factors.\(^\text{7, 12,17,18,19}\) The risk can be multiplied for individuals who have several of these risk factors. See Table 1 for details.
### Table 1: Risk Factors in Melanoma


<table>
<thead>
<tr>
<th>Category</th>
<th>Risk Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nevi</strong></td>
<td></td>
</tr>
<tr>
<td>Dysplastic Nevi</td>
<td>Presence and number of atypical/dysplastic nevi: the presence of a solitary dysplastic nevus doubled the risk of developing melanoma while having 10 or more dysplastic nevi was associated with a 12-fold elevation of risk.</td>
</tr>
<tr>
<td>Melanocytic Nevi</td>
<td>Significant number of melanocytic nevi (more than 50) is a relative risk factor for developing melanoma of 5-fold or greater.</td>
</tr>
<tr>
<td>Other</td>
<td>Unusual in colour or shape</td>
</tr>
<tr>
<td></td>
<td>Large (giant) congenital nevi (&gt;20 cm diameter in an adult)</td>
</tr>
<tr>
<td></td>
<td>Presence of a changing mole or evolving lesion on the skin</td>
</tr>
<tr>
<td><strong>Phenotype</strong></td>
<td>A fair-skin phenotype (blue/green eyes, blond or red hair, light complexion), sun sensitivity (e.g. burns easily, never tans), freckling.</td>
</tr>
<tr>
<td><strong>Personal History</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>A personal history of a previous melanoma is a relative risk of 5-fold or greater of developing another melanoma.</td>
</tr>
<tr>
<td></td>
<td>A history of blistering or severe sunburn(s) in childhood and adolescence, and/or excessive sun exposure</td>
</tr>
<tr>
<td></td>
<td>A personal history of non-melanoma skin cancer or premalignant lesions such as actinic keratoses is approximately a 4-fold increase in risk in developing melanoma.</td>
</tr>
<tr>
<td><strong>Family History of Melanoma</strong></td>
<td>Family history of melanoma in a first-degree relative corresponds to approximately a 2-fold increase in risk for developing melanoma. This risk is higher if more than one relative had a melanoma, if they were young at the time or if one relative had more than one melanoma.</td>
</tr>
<tr>
<td><strong>Other Risk Factors</strong></td>
<td>Immunosuppression (4-to 5-fold increased risk)</td>
</tr>
<tr>
<td></td>
<td>Age (&lt;30 or &gt;50)</td>
</tr>
<tr>
<td></td>
<td>Sex (higher rates in men than in women)</td>
</tr>
</tbody>
</table>

Health professionals are encouraged to assess each individual’s unique risk factors for all skin cancers (personal and environmental) and provide clinical advice tailored to the individual. Those at higher risk may benefit from monthly skin self-examinations and should be advised to become familiar with the pattern of moles, freckles, and other marks on their skin. Patients should be encouraged to report any changing lesions to their health care provider.
2. Management Algorithms

This section contains algorithms providing an overview of the Management of Stage IA and Stage IB-III, Treatment of Local Recurrence and Management of Stage IV Melanoma. Refer to the appropriate section of the guideline for more detail.
Stage IA lesion confirmed
(T1a ≤1.0 mm thick, no ulceration and mitosis <1/mm²)

Pre-operative Metastatic Work-up – to occur within 1 month of lesion confirmation
- Complete History including sun exposure
- Physical exam with attention to locoregional area and draining lymph nodes
- Complete skin exam
- Document family history of melanoma
- Further imaging (CT, MRI) only to evaluate specific signs and symptoms

Follow-up and Surveillance
- History and physical examination, with emphasis on nodes and skin, every 3-6 months years 1-3, and every six months years 4-5
- Educate patient on monthly skin exam, lymph node exam, and signs of locoregional recurrence
- Routine investigation is indicated; imaging for specific signs or symptoms only
Stage IB, II or III lesion confirmed
Stage IB: T1b ≤1.0 mm thick, with ulceration OR mitosis ≥1mm²
Stage II: >1 mm thick, any characteristic but no nodal involvement
Stage III: any T, nodal involvement

Pre-operative Metastatic work-up to occur within 1 month of confirmation
- Complete History including sun exposure
- Physical exam with attention to locoregional area and draining lymph nodes
- Complete skin exam
- Document family history of melanoma
- Chest X-ray for tumours >4mm; optional for other tumours
- Further imaging (CT, MRI) to evaluate specific signs and symptoms
- Consider discussion of Sentinel Lymph Node Biopsy (SNLB)

For Stage III
- Consider imaging of the abdomen and chest (CT or x-ray) as baseline
- LDH (optional)

Follow-up and Surveillance
- History and physical examination, with emphasis on nodes and skin every 3 months for years 1-3, then every 6 months for years 4-5
- Consider annual follow up thereafter as clinically indicated
- Educate patient on monthly skin exam, lymph node exam, and signs of locoregional recurrence
- Further investigations should be based on specific signs or symptoms
Local recurrence often presents as subcutaneous nodule arising in close proximity (within 2 to 5 cm) to an excision site of a primary melanoma (satellite metastasis) or en route to the regional lymph node basin (in-transit metastasis).

- Fine needle aspiration biopsy
- Excisional biopsy under local anesthesia may be required for diagnostic confirmation

Complete metastatic work-up including CT +/- MRI

- Consider referral to specialist surgeon or multidisciplinary team

**Not amenable to surgery**

- Complete surgical resection +/- chemotherapy or radiation
  - Consider isolated hyperthermic limb perfusion when extensive, recurrent satellite or in-transit metastases confined to a single extremity +/- surgical excision of in-transit metastases and regional lymph node dissection.

**Consider referral to palliative care, medical or radiation oncology for palliative measures**
**Figure 4: Metastatic Disease**

- **Metastatic disease identified**
  - Consult to multidisciplinary clinic
  - Refer to palliative care

  **Resectable?**
  - YES
    - Resect with appropriate margins
    - Observation
  - NO
    - Consider clinical trial
    - Palliative Chemotherapy
    - Palliative radiotherapy for symptom management

**Follow Up and Surveillance**

Follow by multidisciplinary team that ideally includes dermatologist, surgeon, oncologist and family physician.

- History and physical examination, with emphasis on nodes and skin every 3 months or at the discretion of the physician
- Educate patient on monthly skin exam, lymph node exam, and signs of locoregional recurrence
- Further investigations should be based on specific signs or symptoms
3. Diagnosis

Many benign skin conditions resemble skin cancers and may be difficult to distinguish clinically. Appendix IV outlines some of the most commonly encountered benign lesions that resemble cancers and a basic triage algorithm to serve as a general guideline for clinical decision making when faced with a lesion that could possibly be skin cancer.

2.1 Sub-Types

Four clinical and pathologic subtypes of melanoma have been identified. The most salient features of each are outlined in Table 2.
Table 2  Comparisons of Clinical Features of Cutaneous Melanoma

<table>
<thead>
<tr>
<th>Type of Melanoma</th>
<th>Frequency</th>
<th>Duration of radial growth phase (years)</th>
<th>Median Age at Diagnosis (years)</th>
<th>Site</th>
<th>Clinical Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superficial spreading melanoma</td>
<td>70%</td>
<td>1-7</td>
<td>44</td>
<td>Any site; lower legs in females, back in both sexes</td>
<td>Variation shades: often, brown, black, white, gray</td>
</tr>
<tr>
<td>Acral lentiginous melanoma (including Subungual melanoma)</td>
<td>5-10%</td>
<td>1-3</td>
<td>65</td>
<td>Sole, palms, Subungual</td>
<td>Flat irregular border; various shades of dark brown, black</td>
</tr>
<tr>
<td>Lentigo maligna melanoma</td>
<td>5%</td>
<td>3-15+</td>
<td>65</td>
<td>Sun-exposed sites including nose, cheeks, temples</td>
<td>Highly irregular border with areas of regression; brown-tan macular lesion with variation in pigment pattern; may be amelanotic</td>
</tr>
<tr>
<td>Nodular Melanoma</td>
<td>15%</td>
<td>Theoretically no radial growth phase</td>
<td>53</td>
<td>Any site</td>
<td>Nodule arises in apparently normal skin or in a nevus; brown to brown-black; may have bluish hues; may be amelanotic</td>
</tr>
</tbody>
</table>

2.2 Diagnosis

Any skin lesion which changes should be assessed. Melanomas often present with a history of a preexisting lesion which changes in some way: increases in size, becomes symptomatic, etc. A change in a pre-existing nevus, a new, pigmented lesion appearing in an adult, or the development of any symptoms (itching) or signs

---

1 Some consider ALM a “hidden” melanoma because it develops in places not easily examined or not thought necessary to examine. ALM is found on the palms and soles; underneath nails; and on mucous membranes, such as those that line the mouth, nose, and anus. In its early stages, ALM is often overlooked because it looks like a bruise or nail streak.
(enlargement, asymmetry, darkening, bleeding, ulceration) should prompt referral for assessment of a pigmented lesion and usually biopsy. The most common change noted initially in early melanoma is increased size (diameter) and color change.

The vertical thickness of the primary tumor is the most important factor in determining prognosis of primary (nonmetastatic) melanoma; increasing thickness of melanoma portends a progressively worse prognosis. As a result, an early diagnosis of melanoma and prompt surgical excision is the most important principle in cutaneous melanoma management.

Early detection of melanoma is facilitated by application of the **ABCDE** rule to any patient with a pigmented lesion:

- **A**symmetry
- **B**order irregularity
- **C**olor variegation
- **D**iameter greater than 6 mm and
- **E** for “evolving”, rather than elevation.

Evolving denotes: change in size, shape, symptoms (itch, tenderness), surface change (e.g. bleeding), or color shade change. This is especially critical for nodular melanomas with predominant vertical growth phase or amelanotic melanomas which present with little or no pigment.\(^{21}\) As the ABCD rule is best applied to early melanomas, E for elevation may not characterize an early lesion.\(^{20}\)

The limitations of the ABCDE rule should be considered so as not to misdiagnosis nodular melanomas with predominant vertical growth phase or amelanotic melanomas which present with little or no pigment.

The **seven point checklist** has also been validated as a screening tool for early melanoma.\(^{7,21,22}\)

**Major features** include:
1. change in size
2. change in color
3. change in shape

The presence of **any** major feature should prompt consideration for removal of lesion or referral.

**Minor features** that may increase suspicion of melanoma include:
4. diameter >6 mm
5. sensory change (itch, altered sensation)
6. inflammation (red tinge in lesion)
7. oozing, crusting or bleeding.

As approximately half of melanomas are detected by patients, self-examination and education about ABCDE’s should be emphasized in any patient with moles, and in particular with specific risk factors for melanoma.

Melanomas detected by physicians are consistently thinner than those detected by a patient or family member, thus the value of a complete, physician-directed skin exam should not be underestimated. Dermoscopy with a hand-held device enhances visualization of pigmented lesions and improves the diagnostic accuracy for melanoma, provided individuals have received specific training in this technique.\(^7\)
In patients presenting with a suspicious skin lesion, a complete history of the evolution of the lesion, sun exposure history, family history and previous skin cancer history is important. The suspicious skin lesion should be biopsied as soon as possible and results discussed with the patient and further treatment planned. Referral to other members of the melanoma interdisciplinary team is arranged as necessary.

2.3 Proper Biopsy Technique

- Any pigmented lesion in which the diagnosis of melanoma is suspected should be biopsied.

- Where practical, a complete excision with narrow margins is recommended.

- An incisional biopsy or punch biopsy may be performed when the lesion is large and complete excision cannot be easily performed.

- A biopsy of the lesion should remove the most raised area, if raised, and the darkest area, if flat.

Lesions suspicious for malignant melanoma must be biopsied to confirm the diagnosis in a timely fashion. When melanoma is suspected, a narrow elliptical excision (margins less than 3mm) that removes the entire tumor should be performed and there are few circumstances that would justify deviation from this practice.

Biopsying a portion of a suspicious lesion, particularly without providing sufficient clinical background to the pathologist (e.g. size of overall lesion, primary vs recurrent lesion, portion biopsied) risks inaccurate interpretation and medical error. Shave biopsies may transect the lesion and incompletely indicate the depth of the lesion and are not preferred. As well, shave biopsies are slower to heal and therefore may delay definitive care of the melanoma.

An incisional biopsy or punch biopsy may be performed when the lesion is large and complete excision cannot be easily performed.

Where a larger lesion precludes complete excision, a representative elliptical biopsy of the most suspicious portion may be considered, provided the treating physician considers potential for sampling error and alteration of accurate final Breslow depth.

Punch biopsies of pigmented lesions cannot provide accurate assessment of architecture or pattern needed to diagnose melanoma. They are best avoided with the following exceptions: 1.) the entire pigmented lesion can be removed with the biopsy, 2.) where complete removal of a larger lesion would produce disfigurement or is anatomically challenged e.g. head and neck or digit, and 3.) the suspicion for melanoma is low.

Shave biopsies may transect the specimen, may miss melanomas involving deeper dermis and may incompletely sample the periphery of the lesion. Given the inherent
risks with this method, it should be utilized only in limited circumstances (as per guidelines for punch biopsy) or avoided entirely.

If the diagnosis of melanoma is equivocal with lesional biopsy, complete surgical excision is warranted by the treating physician or appropriate specialist. It is recommended that excisional biopsy of extremity lesions be oriented longitudinally to facilitate both subsequent re-excision of a melanoma and sentinel lymph node biopsy, when indicated.

Definitive excisional margins will be determined based on accurate measurement of melanoma thickness i.e. Breslow depth, after the entire lesion is excised.

Biopsies of pigmented lesions involving nail beds should be referred to a specialist with experience in nail bed biopsies.

Requisitions accompanying biopsies should include size of lesion, anatomic location of biopsy site and type of procedure performed (eg incisional, vs excisional). 7, 25, 26

2.4 Preoperative metastatic work-up

The assessment for all patients with melanoma should include the following:
- Complete history including sun exposure
- Physical with attention to locoregional area, draining lymph nodes
- Complete skin exam
- Family history of melanoma, prior primary melanoma, atypical nodes, or dysplastic nevi 25

Routine investigations in asymptomatic patients with Stage I and II melanoma are inconsistently used. Blood tests do not yield relevant information and imaging such as Chest X-ray (CXR) or CT scans produce high-false positive results and low incidence true positives for occult metastases. 7,23,25,26, 27

Patients with Stage III disease can be considered for baseline imaging including CXR, CT (abdominal, chest), although the yield of detecting occult metastatic disease remains low. Patients with thick, ulcerated melanomas or large tumor burden in sentinel nodes would be more likely to have true positive findings confirmed by baseline imaging. Imaging to evaluate specific findings from physical exam or symptoms from history that suggest metastatic disease is more likely to yield true positive findings.

PET/CT scan may be useful to confirm metastatic spread in more advanced disease when clinically suspect and to evaluate disease recurrence. 7, 25, 26,27

See Section 3 for a description of melanoma staging.
### Table 3: Stage-specific Additional Work-up

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>Recommended Work Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>in situ</td>
<td>None&lt;sup&gt;25&lt;/sup&gt;</td>
</tr>
<tr>
<td>Stage IA</td>
<td>≤1 mm thick, without ulceration and mitosis &lt;1/mm&lt;sup&gt;2&lt;/sup&gt;</td>
<td>• Further imaging (CT scan, MRI) to evaluate specific signs or symptoms</td>
</tr>
<tr>
<td></td>
<td>Clark level II-III</td>
<td>• Consider discussion of sentinel node biopsy&lt;sup&gt;25&lt;/sup&gt;</td>
</tr>
<tr>
<td>Stage IB</td>
<td>≤1 mm thick with ulceration and mitosis ≥1/mm&lt;sup&gt;2&lt;/sup&gt;</td>
<td>• Chest x-ray optional (for tumours &gt;4 mm, baseline chest x-ray is indicated)</td>
</tr>
<tr>
<td>(intermediate</td>
<td>Clark level IV, V</td>
<td></td>
</tr>
<tr>
<td>risk primary)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage II</td>
<td>&gt;1 mm thick, any characteristic</td>
<td>• Chest x-ray optional (for tumours &gt;4 mm, baseline chest x-ray is indicated)</td>
</tr>
<tr>
<td>(high risk</td>
<td>no nodal involvement</td>
<td>• Further imaging to evaluate specific signs or symptoms for Stage IIB, IIC patients (CT scan, MRI)&lt;sup&gt;25&lt;/sup&gt;</td>
</tr>
<tr>
<td>primary)</td>
<td>Clark level IV, V</td>
<td></td>
</tr>
<tr>
<td>Stage III</td>
<td>sentinel node positive</td>
<td>• Consider baseline imaging (abdominal/chest imaging: x-ray, CT) and to evaluate specific signs or symptoms.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• LDH&lt;sup&gt;25&lt;/sup&gt;</td>
</tr>
<tr>
<td>Stage III</td>
<td>clinically positive nodes</td>
<td>• FNA preferred, if feasible, or lymph node biopsy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Consider baseline imaging (abdominal/chest imaging: x-ray, CT) and to evaluate specific signs or symptoms.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• LDH&lt;sup&gt;25&lt;/sup&gt;</td>
</tr>
<tr>
<td>Stage III</td>
<td>in-transit</td>
<td>• FNA preferred, if feasible, or biopsy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Consider baseline imaging (abdominal/chest imaging: x-ray, CT) and to evaluate specific signs or symptoms.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• LDH&lt;sup&gt;25&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
| Stage IV | Metastatic | • CXR or chest CT  
• CT abdominal and pelvis  
• CT or MRI of head  
• Serum LDH should be performed with confirmed Stage IV disease given prognostic value. \(^{7,25,26,27}\)  
• PET/CT is superior to other diagnostic tests to evaluate for more distant metastasis |
4. Pathology and Staging

The goals of histopathological assessment are to establish a diagnosis and, in the case of a primary melanoma, to comment on relevant prognostic factors. Most important among these are the thickness of the lesion, the presence or absence of ulceration, the mitotic rate in thin (≤1mm in thickness) melanomas, the presence or absence of microsatellites and the status (involved or uninvolved) of the surgical margins.

Microscopic interpretation of pigmented lesions is sometimes challenging and a specialized referral centre, operated by pathologists with particular expertise in the subject, is an important resource. In cases in which the diagnosis is not clear, a second opinion should be sought.

The gross and microscopic evaluation of biopsies and excisions of pigmented skin lesions requires a consistent and systematic procedural approach. In most circumstances, a conservative elliptical excision of skin containing the pigmented lesion should be submitted to the pathology department for diagnostic purposes.

The macroscopic details of the specimen and lesion will be documented and the margins inked. The specimen will be dissected in ‘breadloaf’ fashion to enable a thorough examination of the lesion, and assessment of all surgical margins.

More complex surgical excisions require a specifically tailored approach to gross dissection and these are addressed in the Capital Health Division of Anatomical Pathology Policies and Procedures. A copy of these can be obtained from the Capital Health Division Head of Anatomical Pathology.

In assessing sentinel/regional lymph nodes the finding of a single metastatic melanoma cell (by H&E or immunohistochemistry) implies positivity. In evaluating regional lymph node basins the number of positive nodes should be documented.

See Appendix III for the recommended Surgical Pathology Report template for Primary Invasive Malignant Melanoma.

The 7th edition of the American Joint Committee on Cancer (AJCC) Staging Manual was released in 2010, and included changes for the staging of melanoma. Key points include:

(i) For patients with localized (stage I or II) melanoma, tumor thickness, mitotic rate and ulceration are considered the most powerful prognostic indicators

(ii) Clark’s level of invasion was replaced by mitotic index for patients with thin (≤1 mm) primary tumors

(iii) All patients with microscopic nodal melanoma metastases (including those with only 1 cell identified) are classified as stage III

(iv) For patients with regional lymph node metastases, the number of lymph nodes involved, metastatic tumor burden, and ulceration and thickness of the primary tumor were the most predictive independent factors of survival

(v) For patients with distant metastases, the site (non-visceral vs lung vs other visceral) and serum LDH elevation continue to define the M category

Practical Implications for the Pathologic Reporting of Melanoma Cases

Primary lesion
(i) In thin melanomas (≤1mm in thickness) the mitotic rate (< 1 mitosis/mm²; or ≥1 mitosis/mm²) must be provided
(ii) Provision of the Clark level is optional (non-essential) in thin melanomas
(iii) The Breslow thickness, presence or absence of ulceration, status of the margins (involved or uninvolved) and presence or absence of a microsatellite (deposit of melanoma 0.05mm in diameter separated by at least 0.3mm from main tumor) must be recorded as before

Sentinel/Regional Lymph Nodes
(i) The presence of 1 melanoma cell (on H&E or IHC) in a sentinel or regional lymph node implies positivity
(ii) In evaluating regional lymph node basins the number of nodes involved should be documented.
AJCC Staging Classification for Melanoma

Primary Tumor (T)

TX Primary tumor cannot be assessed (e.g., curettaged or severely regressed melanoma)
T0 No evidence of primary tumor
Tis Melanoma in situ
T1a: Melanoma ≤1.0 mm thickness, no ulceration, <1 mitoses/mm²
T1b: Melanoma ≤1.0 mm in thickness with ulceration or ≥1 mitoses/mm²
T2a: Melanoma 1.01 to 2.0 mm in thickness, no ulceration
T2b: Melanoma 1.01 to 2.0 mm in thickness, with ulceration
T3a: Melanoma 2.01 to 4.0 mm in thickness, no ulceration
T3b: Melanoma 2.01 to 4.0 mm in thickness, with ulceration
T4a: Melanoma greater than 4.0 mm in thickness, no ulceration
T4b: Melanoma greater than 4.0 mm in thickness, with ulceration

Regional Lymph Nodes (N)

NX Regional lymph nodes cannot be assessed (e.g., previously removed for another reason)
N0 No regional metastases detected
N1-N3 Regional metastases based on the number of metastatic nodes and presence or absence of intralymphatic metastases:
N1 Metastasis in one lymph node
N1a micrometastasis
N1b macrometastasis
N2 Metastasis in two to three regional nodes or intralymphatic regional
N2a micrometastasis
N2b macrometastasis
N2c Satellite or in-transit metastasis without metastatic nodes
N3 Four or more metastatic nodes, or matted nodes, or in-transit metastasis or satellite(s) with metastatic node(s)

Distant Metastasis (M)

M0 No detectable evidence of distant metastasis
M1a Metastases to skin, subcutaneous or distant lymph nodes
M1b Metastases to lung
M1c Metastases to all other visceral sites or distant metastases to any site combined with an elevated serum lactic dehydrogenase (LDH)

Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original and primary source for this information is the AJCC Cancer Staging Manual, Seventh Edition (2010) published by Springer-Verlag New York. (For more information, visit www.cancerstaging.net.) Any citation or quotation of this material must be credited to the AJCC as its primary source. The inclusion of this information herein does not authorize any reuse or further distribution without the expressed, written permission of Springer-Verlag New York, Inc., on behalf of the AJCC.

Anatomic Stage/Prognostic Groups (Clinical staging*)
Clinical staging includes microstaging of the primary melanoma and clinical/radiologic evaluation for metastases. By convention, it should be used after complete excision of the primary melanoma with clinical assessment for regional and distant metastases.

Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original and primary source for this information is the AJCC Cancer Staging Manual, Seventh Edition (2010) published by Springer-Verlag New York. (For more information, visit www.cancerstaging.net.) Any citation or quotation of this material must be credited to the AJCC as its primary source. The inclusion of this information herein does not authorize any reuse or further distribution without the expressed, written permission of Springer-Verlag New York, Inc., on behalf of the AJCC.

**Genetics**

Several genes have been linked to increased melanoma risk, including CDKNZ, CDK4, and MCIR. However, the most important gene associated with melanoma is BRAF, which regulates several signaling pathways involved in cell division, differentiation, and secretion. Reported a mutation in BRAF in 66% of malignant melanomas. This oncogene may play a critical role in our understanding of malignant melanoma and has been the focus of most new research into melanoma treatments. Recently, a prospective observational study involving BRAF-tested patients with metastatic melanoma identified BRAF mutations in 48% of patients, of which 74% had V600E, 20% had V600K, and 6% had other genotypes. While BRAF mutations may be associated with poorer survival, it seems the presence of mutant BRAF had no impact on the interval from diagnosis of primary melanoma to first distant metastasis.

**Prognostic Factors for Melanoma:**
Health professionals should help patients and families understand the prognosis of melanoma so that they can make appropriate informed decisions about their treatment.

Melanoma stage is correlated with survival. Early stage disease as calculated by TNM has better prognosis than late stage disease. In addition to stage, certain clinical and histological prognostic factors have been identified.

Clinical factors
- Sex: Female sex confers a better prognosis
- Age: Older patients have a poorer prognosis
- Anatomic location: Extremity melanomas have a better outcome than truncal or scalp melanomas

Histological factors:
- Thickness: The vertical thickness of the primary tumor as measured by Breslow\textsuperscript{31} is the most important histologic factor in determining prognosis of primary (non-metastatic) melanoma; increasing thickness of melanoma portends a progressively worse prognosis.

- Nodes Involved: The number of nodal metastases is also a prognostic indicator. With only 1 node involved, the prognosis is comparatively better than when more than 2 nodes are involved.

- Ulceration: The presence of ulceration confers a poorer outcome.

- Mitoses: The greater the number of mitoses, the poorer the prognosis.

Metastases:
- Distant metastases usually indicate a poor prognosis.

Other:
- Tumour-infiltrating lymphocytes are believed to be a favourable prognostic feature, whereas histologic regression is believed to portend a poorer prognosis.\textsuperscript{32}

- Elevated serum LDH at the time of initial Stage IV diagnosis is an independent and highly significant predictor of poorer survival outcome among patients who present with or develop Stage IV.\textsuperscript{28}
Surgical Treatment of Primary Melanoma

Treatment goals and prognosis should be reviewed regularly with patients and revised as necessary. The standard of care in the management of cutaneous malignant melanoma is complete excision of the primary lesion with an appropriate margin of normal tissue.

Primary Lesion:

Primary wide excision of the melanoma is the standard of care in the vast majority of newly diagnosed melanoma. In rare circumstances such as a lentigo maligna melanoma, a course of radical radiotherapy can be attempted if the resection of the primary lesion would result in a substantial loss of function or an unacceptable cosmetic result.

Sentinel lymphadenectomy is performed most accurately at the time of wide definitive excision of the primary melanoma. (see Section 5 for more detail). Sentinel lymphadenectomy must be done at an appropriately equipped facility with surgical and pathology staff who have received appropriate training in the procedure.

Current recommendations for resection margins are (See Table 4.1):

a) Malignant melanoma in situ is excised with 0.5 cm margins. Lentigo maligna histologic subtype may require greater than 0.5 cm margins as these lesions may have a broad subclinical extension.

b) Thin (<1 mm) melanomas have an extremely low rate of local recurrence (<2%) and are excised with 1 cm margins.

c) For intermediate-thickness (1 to 4 mm) lesions, the safety of 2 cm excision margins has been confirmed in prospectively randomized studies.

d) For thick melanomas (>4mm), 2.0 cm margin

See Appendix I for more details about resection margins.

Excision sites are most often closed primarily, although split- or full-thickness skin grafting or flap closure may be required for the reconstruction of larger defects.

Satellite lesions (within 2 to 5 cm of the primary lesion):

There is little data to guide the management of satellite lesions. Excision should be incorporated into the excision of the primary lesion maintaining the 2 cm margin beyond the radial edge of satellite lesion.
**In-transit lesions** (beyond 5 cm of the primary lesion but between the primary lesion and draining nodal basin):

Complete excision with clear margins and primary closure where possible is recommended.

---

**Table 4.1 : Management of Primary Cutaneous Melanoma**  

<table>
<thead>
<tr>
<th>Breslow Thickness</th>
<th>In-situ</th>
<th>&lt;1 mm</th>
<th>1.01 - 2mm</th>
<th>&gt;2 mm</th>
<th>&gt;4 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical Margin</td>
<td></td>
<td>0.5 - 1.0 cm</td>
<td>1.0 cm</td>
<td>1.0 - 2.0 cm</td>
<td>2.0 cm</td>
</tr>
<tr>
<td>Sentinel Node Biopsy</td>
<td>No</td>
<td>Only with ulceration or mitosis (stage T1b)</td>
<td>Recommended for staging</td>
<td>Recommended for staging</td>
<td>Recommended for staging</td>
</tr>
</tbody>
</table>
5. Treatment of Regional Lymph Nodes

Management of the regional lymph nodes is based on clinical findings and the thickness of the primary lesion.

**Cutaneous melanoma <1 mm in thickness** does not require assessment of regional nodes as the risk of nodal involvement is low (<5%) except for those cases <1mm with Clark’s level IV/V thickness, ulceration or regression or >1 mitosis/mm².

Assessment of the nodal basin in patients with **thick (>4 mm)** melanoma should be made on a case by case basis. Wong et al in their recent guideline³⁹ indicate that SNL biopsy in this population may be recommended for staging purposes and to facilitate regional disease control.

**Cutaneous melanoma 1-4 mm in thickness and clinically negative regional nodes** –

**Sentinel Lymph Node Dissection**

The sentinel lymph node (SLN) is the lymph node which most directly drains the area of skin in which a melanoma has occurred and is most likely to contain micrometastases. Cutaneous lymphoscintigraphy allows for a more precise delineation of the primary lymphatic drainage of cutaneous melanomas and aids in the identification of the sentinel lymph node(s).⁴⁰,⁴¹ Sentinel lymph node dissection is performed as a staging investigation for patients diagnosed with melanomas between 1-4 mm with no clinical evidence of regional lymph node metastases and thin Level IV melanomas and may be used for thin melanomas with poor prognostic features (see above)⁴². (See Appendix II for technical details.)

There is a large body of evidence supporting the sentinel lymph node biopsy (SLNB) as the most sensitive staging tool and, furthermore, that sentinel lymph node (SLN) status is the most important factor for prognosis and survival. The Multi-centre Selective Lymphadenectomy Trial (MSLT) was the first large randomized trial to demonstrate the accuracy of lymphatic mapping/ SLNB technique. The results of this study suggest that disease-free and melanoma-specific survival is higher for patients who have a positive sentinel node biopsy and complete node dissection.⁴³

Despite these findings there is still considerable controversy regarding whether SLN status can accurately predict prognosis. Specifically, there is evidence to suggest that not all positive SLNs, especially ones with micrometastatic disease, will progress to clinically relevant disease, resulting in “prognostic false positive”.⁴⁴

Sentinel lymph node biopsy (SLNB) is recommended by the American Joint Commission for Cancer (AJCC) as a staging procedure in patients for whom the information will be useful in planning subsequent treatments and specifically in T1b (0.76 – 1.00 mm in thickness) melanoma and upward, with clinically or radiologically uninvolved nodes.²⁸
Wong et al.\textsuperscript{39} note that routine use of SLNB in this population provides accurate staging, with high estimates for proportion of patients successfully mapped, acceptable estimates for false-negative rate, post-test probability negative, and predictive value positive.

Sentinel lymphadenectomy is most accurately performed at the time of definitive excision of the primary melanoma. Consequently, patients who have already undergone definitive wide excision of the primary lesion are not ideal candidates for sentinel lymphadenectomy as evidence to support this practice is lacking. In these situations the application of sentinel lymph node technology must be considered on an individual, case by case basis.

**Evaluation of Sentinel Lymph Nodes from Patients with Melanoma**

Excision and evaluation of sentinel lymph nodes from patients with melanoma enhances the accuracy of staging of the disease. This is done by microscopic evaluation, including immunohistochemistry. The sentinel node (or nodes) should be fixed in formalin and sent to the laboratory. There, the node (or nodes) is (are) bisected, serially sectioned and appropriately stained. Evaluation of the sentinel lymph nodes can be challenging and is best performed by a pathologist with experience in the area. The demonstration of metastatic melanoma in the sentinel lymph node on microscopic examination has a proven adverse prognostic implication and is relevant to the staging of the disease.

**Management of Patients with Positive SLNB**

Patients with positive SLNB should have completion lymph node dissection (CLND) for regional disease control. It is not yet known whether CLND following a positive SLN biopsy improves survival.\textsuperscript{39}

**Elective Lymph Node Dissection**

Most patients with newly diagnosed melanoma exhibit no evidence of regional lymph node metastases.

Patients with intermediate-thickness lesions (1 to 4 mm) have a 10% to 45% incidence of microscopic regional disease and a 3% to 25% risk of distant metastases and should theoretically derive the greatest therapeutic benefit from elective lymph node dissection. Prospectively randomized studies, however, have consistently failed to demonstrate a significant survival advantage with elective lymph node dissection.\textsuperscript{45-53} Nevertheless, the excision of clinically negative, microscopically positive lymph nodes in patients with melanoma may provide valuable staging information and serves to identify those patients at high risk for systemic disease who may be candidates for additional surgical or adjuvant treatment.
**Cutaneous melanoma >1mm thick and clinically positive lymph node metastases**

Any palpable lymph node in a patient with melanoma should be considered indicative of metastasis until proved otherwise. Fine needle aspiration biopsy is an accurate, reliable method of confirming metastatic melanoma. If fine needle aspiration is not available or results are indeterminate, excisional biopsy of the lymph node is performed. Patients presenting with or subsequently developing regional lymph node metastases are at high risk for distant metastases and should undergo advanced scanning with intravenous contrast of the chest, abdomen, and pelvis and CT or MRI scanning of the brain. PET/CT is the most accurate tool for evaluating potential disease recurrence, distant metastasis or extent of metastatic disease.

In general, definitive treatment for highly suspicious lymphadenopathy consists of complete lymph node dissection.

In patients with cytologically or histologically proved regional nodal metastases, formal (complete) lymph node dissection is performed. The development of palpable lymph node metastases is correlated significantly with substantially diminished survival (10% to 50%), which is influenced strongly by the number of and the extent to which the lymph nodes are involved and the primary melanoma thickness.

Regional lymph node dissection should not be performed routinely in patients with documented distant metastases that are extensive or in those patients with large lymph node metastases fixed to adjacent structures. Significant palliation of inoperable bulky or bleeding regional nodal metastases may be achieved with radiation therapy in such situations, which are associated with an extremely poor prognosis.
7. Adjuvant Therapy for High Risk, or Advanced Melanoma

Overview
The management of regional metastatic disease is dependent on the number and location of metastatic lesions. Generally, isolated lesions may be surgically excised. Patients with regional lymph node involvement may consider therapeutic lymph node dissection or adjuvant therapy. Patients with extensive metastases (Stage IV) may undergo chemotherapy, radiation therapy, biologic therapy or combination therapy.

See Figure 4: Management of Metastatic Disease page 9.

Chemotherapy
The only standard adjuvant chemotherapy approved for the treatment of resected malignant melanoma is interferon. While interferon appears to have an impact on melanoma, the use of interferon in an adjuvant setting is controversial. Evidence from two of three randomized trials by ECOG suggests interferon may prolong disease-free survival but not overall survival in high-risk melanoma patients. Other randomized trials have not shown this.

Interferon alfa 2b is currently offered to patients with high risk disease, provided that each patient has been made aware of the relative risks and benefits. High-risk is defined as patients in the following clinical states who have been rendered disease free by surgery:
- T4 N0 or any T N1, 2, 3
- Involved nodes were excised with no primary cutaneous lesion.

High-dose interferon alpha therapy includes four weeks IV therapy administered at a hospital followed by patient self-administration subcutaneously three times weekly for 48 weeks at home. The interferon for home administration must be acquired by the patient through their retail pharmacy.

Treatment risks are significant, with 67% of trial patients experiencing severe toxicity, and 9% having life-threatening toxicity. Toxicities included grade 3 flu-like symptoms, elevated liver enzyme levels with lethal hepatotoxicities, neurologic and neuropsychiatric symptoms, and a rare lethal rhabdomyolysis.

Because of the significant cost and toxicity associated with the use of Interferon alfa 2b, patients who are candidates for consideration should be referred to medical oncology for review and discussion of the risks and benefits.
Trials with interferon in combination or comparison with other adjuvant agents (e.g., melanoma vaccines) and other adjuvant therapies are ongoing. Patients should be considered for available clinical trials, when appropriate.

Current treatment recommendations are:

Stage I A, I B, I I A, I I B (T3bN0) – no adjuvant therapy
Stage I I B, I I C (T4a or b, N0) – observation or interferon alfa 2b
Stage III – observation or interferon alfa 2b

Radiotherapy

Radiotherapy dose and fraction size for melanoma remains controversial. It has been suggested from retrospective studies that a high dose per fraction can result in better local control.

The use of radiotherapy in the postoperative setting has been shown to improve local control but there is no evidence for survival benefit. Post-operative radiotherapy could be considered in the following circumstances:
- Positive or close resection margin when re-excision is not possible
- Gross residual disease
- Multiple positive lymph nodes or single node 2.5 cm in size or greater
- Extra nodal or soft tissue extension

Monitoring Response to Therapy and Reassessment of Disease

FDG PET/CT is the most accurate method of assessing treatment response.
8. **Treatment of Local Recurrence**

Local recurrence in a patient with malignant melanoma is an ominous clinical event and is almost always associated with the development of systemic metastases. The survival of these patients is extremely poor averaging less than 5% at 10 years. Local recurrence most often appears clinically as a blue-tinged subcutaneous nodule arising in close proximity (within 2 to 5 cm) to an excision site of a primary melanoma (satellite metastasis) or en route to the regional lymph node basin (in-transit metastasis). Any subcutaneous nodule arising in the vicinity of a melanoma excision site should be considered to be disease recurrence or progression until proved otherwise.

Diagnosis is made by fine needle aspiration biopsy. Excisional biopsy of the nodule under local anesthesia may sometimes be required for diagnostic confirmation. If this is felt to be indicated, referral to a surgeon who treats patients with melanoma is recommended.

Following confirmation of recurrence, a complete metastatic survey, including CT and/or MRI and/or PET/CT should be performed because most of these patients will now also have evidence of systemic metastases. Referral to the palliative care team should also be considered and advanced care planning discussed with the patient and family.\(^{33}\)

See Figure 3, page 8.
Work Up for Recurrences

True local scar recurrence
- Biopsy to confirm
- Chest x-ray optional
- CBC, LDH optional
- CT scan, PET/CT*, MRI, as indicated

Local, satellitosis, and/or in-transit recurrence
- FNA (preferred) or excisional biopsy
- Chest x-ray and/or chest CT
- Pelvic CT if inguinal nodes clinically positive
- PET/CT*
- Other CT scans or other imaging studies if clinically indicated
- CBC, LDH optional

Nodal recurrence
- FNA (preferred) or lymph node biopsy
- LDH
- Chest x-ray and/or chest CT
- Pelvic CT if inguinal nodes clinically positive
- Abdominal and pelvic CT ± MRI head, PET/CT scan* as indicated

Distant recurrence
- FNA (preferred) or biopsy
- LDH
- Chest x-ray and/or chest CT
- Abdominal/pelvic CT, MRI brain, PET scan* as indicated

* PET/CT is the most accurate tool for evaluating potential disease recurrence, distant metastasis or extent of metastatic disease. In the scenario of patients who have had significant nodal dissections, PET/CT is superior for evaluating potential in transit disease or local node recurrence because of underlying scar and other post treatment change.

Surgical treatment of locally recurrent malignant melanoma

Although no standardized surgical approach to all patients with locally recurrent melanoma has been established, treatment guidelines have been developed based on clinical trials in patients selected by the extent and specific anatomic site of disease recurrence. The realization that local recurrence is not simply the result of inadequate surgical excision but is in fact an outward manifestation of the biologic aggressiveness of the primary melanoma has led to a more rational approach to the treatment of these patients.

Complete surgical resection with primary wound closure is the most straightforward means of treating single recurrent lesions. Patients with multiple
subcutaneous metastases grouped within a single site can similarly be treated with wide local excision with skin grafting or flap closure as necessary for wound coverage. Although wide resection margins are not as well defined in the resection of locally recurrent disease as they are in the treatment of primary cutaneous melanoma, recurrent lesions should be resected with a margin of normal tissue to avoid tumor spillage and wound contamination. Fracturing of the tumor mass is often followed by further rapid local recurrence.

Despite complete surgical resection of multiple cutaneous metastases, further local and regional recurrence may occur in up to 67% of patients and is strongly associated with subsequent disease progression. As many as 70% to 82% of such patients ultimately succumb to distant metastases. 63

Of all patients with stage I to III completely resected melanomas, 30% develop a recurrence. Overall, among patients whose melanoma recurs, 20% to 28% first recur with local or in-transit disease, 26% to 60% with regional nodal disease, and 15% to 50% with distant metastases. When melanoma recurs locally, in-transit, or in regional nodal basins, approximately one-third of patients can be cured with additional treatment.64

Isolated hyperthermic limb perfusion

Non-resectable in-transit metastases or inoperable primary tumours confined to an extremity may be treated with isolated limb perfusion. 65 Such treatment is highly specialized. Patients who might benefit should be referred to the Melanoma Cancer Site Team at the QEI. (See Section 14.)


9. **Treatment for Distant Metastases (Stage IV Melanoma)**

Melanoma is the third most common cause of metastases to the central nervous system. About 2/3 of these are multiple; the other third are solitary metastases.

The aims of therapy in stage IV melanoma must be clearly defined and generally include one or more of the following: (1) to relieve symptoms of a life-threatening problem, (2) to increase length of survival and (3) to evaluate new therapies. Survival is dependent on the sites of metastatic disease and on the volume of disease. Cutaneous and pulmonary metastatic disease tend to have a longer survival than other sites.

The management of the patient with distant metastatic melanoma must take into account several important factors. Modalities include chemotherapy, immunotherapy and combined therapy with varied results. Because of the limited efficacy, therapy should be individualized and consider the age, underlying medical condition of the patient, number and site(s) of metastasis, previous treatments, and the wishes of the patient and family. 33

Palliative care and advanced care planning should be considered early in the care path for patients with Stage IV (metastatic disease). 33

**Surgery**

Surgical excision of isolated metastases in certain sites such as the skin and subcutaneous tissue, lymph nodes, lung, brain and gastrointestinal tract can prolong survival. The number of metastatic lesions has prognostic importance with patients having a solitary lesion performing relatively better than those with 2 or more sites. Excision of metastatic lesions can achieve significant palliation. These patients should be referred to a surgical oncologist.

**Radiation Therapy**

Radiotherapy should be considered for patients with unresectable metastatic melanoma. Radiation is most commonly used for patients with advanced axillary or groin disease, brain metastasis and extensive cutaneous lesions not amenable to surgery. Radiation remains the primary treatment modality for symptomatic bone metastases.

**Chemotherapy**

The standard therapy with single agent Dacarbazine can be offered. Other therapies including combination chemotherapy with Decarbazine and chemotherapy with immuno-therapies have not been shown to provide advantage over single agent Dacarbazine and do increase the toxicity.

Interleukin 2 is associated with prolonged complete remission in approximately 5% of patients. This therapy is currently not available in Nova Scotia.
Temozolomide, the oral pro drug of Dacarbazine, offers similar response rates to Dacarbazine (i.e. 15-20% and no improvement in overall survival) but offers the convenience of an oral medication. It is not approved in Nova Scotia for treatment for metastatic melanoma. Some third party payers will finance the drug.

Patients who have unresectable metastatic disease should be considered for any clinical trials which are open.

**Recommended Treatment for Metastatic Disease: (See Figure 4)**

**Resectable** – resect with appropriate margins (see Table 4.1) with observation.

**Unresectable:**
- Consider clinical trial
- Dacarbazine or temozolomide
- Cisplatin or paclitaxel as second line chemotherapy if Performance Status is 0-2.
- Radiation remains the primary treatment modality for symptomatic bone metastases
- Radiotherapy for brain metastases, advanced axillary or groin disease and extensive cutaneous lesions not amenable to surgery

New systemic therapies are emerging for metastatic melanoma. Each of these treatments are promising but still carry low response rates and are often not long-lasting responses. Participation in clinical trials is encouraged when available.

These include:

- **vemurafenib** as first line for patients who carry the BRAF mutation(approximately 40%). Testing for this marker is performed out of province at this time.
- **Dacarbazine** remains the standard chemotherapy first line for patients who do not carry the BRAF mutation.
- **Ipilimumab**, an immune modulator, is available as second line for patients who qualify based on performance status and absence of other autoimmune disorders.
10. Sub-types Melanoma

10.1. Subungual Melanoma

Subungual melanoma is a rare clinical entity representing up to 3% of cases of melanoma in whites but a higher proportion of melanomas (15% to 35%) in dark-skinned ethnic groups.\textsuperscript{66-68} Over 75% of subungual melanomas involve either the great toe or the thumb.

Early diagnosis of subungual melanoma is rare, with the poor prognosis of this lesion reflecting most significantly advanced stage at diagnosis. Many patients with subungual melanoma report a recent history of trauma to the digit and attribute the lesion to a poorly healing wound.

The major pitfall in the diagnosis of subungual melanoma is an inadequate biopsy. A diagnosis of subungual hematoma may be confirmed by releasing the clotted blood through a large bore puncture or partial removal of the nail plate. Close visual inspection of the nail over a short period of time reveals that the pigmentation advances distally with growth of the nail plate. Formal biopsy of the nail bed is performed under digital or regional anesthesia block in the office or outpatient setting. The nail plate is then elevated carefully from the nail bed and removed so that the proximal aspect of the lesion in question is visualized clearly.

An elliptical incision in the nail bed down to the underlying periosteum is then performed allowing for complete excisional biopsy of the lesion and primary closure of the defect with fine absorbable sutures. Larger defects may be repaired with nail bed flaps or skin grafting. Generous incisional biopsy through the central portion of pigmentation is performed for larger lesions not amenable to simple excision. Melanoma in situ of the nail bed is treated with wide local excision. Negative surgical margins of at least 5 mm are optimal. The surgical defect may be repaired with a local flap of skin or may require skin grafting.

Invasive subungual melanomas of the lower extremity are treated most easily with amputation of the toe. The appropriate surgical resection margin width of 1 or 2 cm for lesions with thickness less than 1 mm or greater than or equal to 1 mm, respectively, is achieved through complete amputation of the affected toe. Ray amputation is performed for lesions extending into the webspace. In most patients, the resulting surgical defect is closed easily, heals well, and allows for ambulation without a specialized prosthesis or orthotic device, even when amputation of the great toe is required.

For upper extremity subungual invasive melanomas, surgical treatment is more individualized. Amputation is performed through the joint most proximal to the lesion, which represents a more conservative and functionally superior approach to the more radical amputations performed in the recent past.\textsuperscript{69} Wound closure is achieved with a flap of volar tissue while ideally maintaining a margin of at least 1 cm of normal tissue.
For subungual melanomas of the thumb, a reconstruction is performed by webspace deepening using a Z-plasty, reducing the length of digit loss by approximately 50%.\textsuperscript{70} Management of draining lymph nodes is based on depth of invasion as in other cutaneous malignant melanoma and should be managed accordingly.

10.2. Plantar Melanoma

Melanoma arising on the sole of the foot is rare in whites accounting for only 2\% to 8\% of melanoma cases. However, it arises on the plantar surface of the foot in 35\% to 90\% of patients diagnosed with melanoma of African-American, Asian, or Hispanic descent.\textsuperscript{71}

The preferred method of biopsy for these difficult lesions is complete excisional biopsy. Definitive wound closure may be deferred until rapid histologic diagnosis and margin inspection are complete.

Once the diagnosis of melanoma is confirmed, the lesion is widely excised and staged according to guidelines established for other cutaneous primary melanomas of comparable thickness. Wound closure of the plantar surface requires special consideration. The exact location of the melanoma on the plantar surface, stage of disease, age, associated medical conditions, and lifestyle of the patient must be considered in the determination of wound closure. Defects on non-weight-bearing aspects of the plantar surface or those in patients with sedentary lifestyles, significant medical co-morbidities, or advanced metastatic disease may be closed most easily primarily or more commonly with split-thickness or full-thickness skin grafts. Closure of defects on the weight-bearing surface of the plantar region in ambulatory patients is accomplished with a variety of flap reconstructive procedures. These include relatively straightforward cutaneous rotational or advancement flaps and more complex reconstructive procedures, such as free microvascular skin or muscle flaps.\textsuperscript{72} These latter procedures usually require a reconstructive plastic surgeon.

Management of draining lymph nodes is based on depth of invasion as in other cutaneous malignant melanoma and should be managed accordingly.

10.3. Melanoma of the Face and Head
10.3.a Melanoma of the Ear

The ear provides a unique challenge because of its anatomy. The ear is a trilaminar structure, with cartilage interposed between two layers of skin. Ideal surgical margins are rarely achieved. Functional considerations must be considered in all cases. Total removal of an ear is rarely recommended.

Closure for small in situ lesions where cartilage is not disrupted may be achieved by small advancement flap but frequently requires full thickness grafting. Larger lesions and invasive lesions require wedge resections with conchal cartilage removal as well.

Lesions < 1 cm will often close primarily with appropriate realignment of cartilage. Larger lesions require more complicated reconstructive surgery. It is recommended that a
plastic and reconstructive surgeon become involved early in the management of these cases to optimize the functional and curative outcome for the patient. See also CCNS Guidelines for the Management of Head and Neck Cancers.

10.3.b Melanoma of the Nose

Nasal surgery and reconstruction for melanoma presents a unique challenge because of the complex anatomy of the nose. It is strongly recommended that all melanoma of the nose be referred to a melanoma team that includes Dermatology, Surgical Oncology, Plastic and Reconstructive Surgery, and Otolaryngology-Head and Neck surgery to plan and execute treatment for melanoma arising in this area. See also CCNS Guidelines for the Management of Head and Neck Cancers.

10.3.c Melanoma on the face

Melanoma occurs rather commonly on the face and most often takes the form of an in situ (Hutchinson’s melanotic freckle or lentigo maligna) or thin invasive lesion. Despite their diminished biologic aggressiveness, however, the cosmetic and functional considerations of performing tumor surgery on the face makes treating even these lesions especially challenging. It is strongly recommended that all melanoma of the face be referred to a melanoma team that includes Dermatology, Surgical Oncology, Plastic and Reconstructive Surgery, and Otolaryngology-Head and Neck surgery to plan and execute treatment for melanoma arising in this area.

Surgical biopsy should be performed to assess melanoma thickness fully to plan definitive surgical treatment of the primary lesion appropriately and determine the risk of regional lymph node metastases and the need for procedures, such as lymphatic mapping and sentinel lymphadenectomy. As in other anatomic locations, complete excisional biopsy is the procedure of choice for confirming the diagnosis of melanoma and to measure lesion thickness. Care should be taken, however, with any biopsy technique chosen, to avoid injury to the branches of the facial nerve. The marginal mandibular division, because of its superficial location and diminutive size, is particularly at risk. The possibility of facial nerve injury should be discussed with the patient and documented appropriately before any biopsy procedure.

All melanomas on the face should be excised with appropriate margins. However, achieving an appropriately wide resection margin may be difficult for melanomas located in close proximity to structures such as the eye, nose, and mouth. A good rule of practice is to obtain as close to as possible the desired surgical margin based on the thickness of the melanoma. As in the case of melanoma involving plantar surfaces and other anatomically challenging areas, management of these cases should involve a team of surgeons experienced with the issues of morbidity and reconstructive surgery often associated with definitive surgery to optimize the functional, cosmetic and curative outcome for the patient.
Patients with melanoma > 1mm with clinically negative lymph nodes should be considered for sentinel lymph node dissection as described in Section 5. The only caveat in this situation is that the lymphatic drainage is very unpredictable in head and neck melanoma. Accordingly, in terms of planning surgery and discussing risk and benefit to the patient, one is often aided by information gained through preoperative lymphoscintigraphy that will define the nodal basin(s) at risk and help plan and schedule appropriate time and resources for the surgery. 36, 75, 76

Regional lymphadonectomy including superficial parotidectomy with dissection of all facial nerve branches is recommended for patients with micrometastases in periparotid nodes. It must be made clear to the patient that the primary motivation for sentinel lymph node dissection in the management of cutaneous malignant melanoma is to more accurately stage the patient’s disease. Accordingly the associated risks and benefits must be discussed and documented, especially in the case of head and neck disease where the risks of nerve injury and functional loss may not justify the benefits of extensive and multiple sentinel lymph node dissections for that patient.

Management of draining lymph nodes is based on depth of invasion as in other cutaneous malignant melanoma and should be managed accordingly.

See also CCNS Guidelines for the Management of Head and Neck Cancers (available at www.cancercare.ns.ca).
11. Melanoma in pregnancy

The overall incidence of melanoma in pregnancy is estimated to be 0.14 to 0.28 cases per 1000 births. Although it is rare to see melanoma in pregnant women, melanoma is one of the most common tumors known to metastasize to the placenta and fetus. Despite the fact that melanocytic nevi commonly become larger and darker under the hormonal influence of pregnancy presumably due to increased levels of estrogen, a melanocyte stimulating hormone, there exists no conclusive evidence that pregnancy significantly affects the biologic aggressiveness of a melanoma in terms of increasing the incidence of metastasis or lowering overall survival. Moreover, pregnancy occurring either before or after the diagnosis and treatment of melanoma similarly seems to have no significant effect on the clinical course of the disease.

Based on the data presently available, the termination of pregnancy of a patient recently diagnosed with melanoma as a therapeutic measure cannot be recommended. Because the overwhelming (75% - 90%) majority of melanoma recurrences happen within 2 to 3 years after treatment of the primary lesion, women of child-bearing age should be encouraged to avoid becoming pregnant for that period of time postoperatively.

The frequent observation that melanocytic lesions may become more pronounced during pregnancy makes the diagnosis of melanoma even more difficult. As in any other patient, however, any cutaneous lesion suspicious for melanoma in a pregnant patient should undergo biopsy without delay. This is preferably accomplished with a complete excisional biopsy, which may be performed safely in the pregnant patient under local anesthesia. Although most of these biopsy procedures may be carried out safely and rapidly in the office setting, the excision of larger lesions may be performed more prudently in the ambulatory surgery unit with an anesthesiologist, knowledgeable in the care of the pregnant patient, in attendance with intraoperative fetal monitoring during the later stages of pregnancy if appropriate.

Once the diagnosis of melanoma is confirmed histologically, an abbreviated metastatic survey may be ordered but surgical treatment is planned commensurate with the thickness of the primary lesion and clinical stage of disease. Radiologic work-up may include radiographs of the chest, which may be performed safely during pregnancy with the appropriate shielding. In patients with palpable regional nodal metastases, sonographic examination of the abdomen and liver may be performed to search for visceral metastases instead of CT scanning with intravenous contrast, which is not recommended during the early stages of pregnancy.

Management of the primary lesion is based on depth of invasion as described in these guidelines and does not change in the pregnant woman.
Formal therapeutic regional lymph node dissection is performed concurrently in the presence of palpable nodal metastases. The treatment of the regional nodes in patients with melanomas greater than or equal to 1 mm thick and no clinical evidence of metastatic disease is less clear. Although intraoperative lymphatic mapping using vital blue dye and radiolabeled technetium sulfur colloid and sentinel lymphadenectomy is currently the accepted approach to non-pregnant patients with melanomas greater than or equal to 1 mm thick and no clinical evidence of nodal metastases, the accuracy and safety of this procedure in pregnant patients has not yet been studied completely and confirmed. The surgical approach to the regional lymph nodes in this group of patients must be individualized with all possibilities discussed in detail with the patient and her family. Because no significant survival advantage has been demonstrated in prospective randomized clinical trials for patients with melanomas undergoing elective regional lymph node dissection, a reasonable approach is wide and deep excision of the primary melanoma and no treatment of the regional nodes at that time. Regional lymph node dissection may be performed at a later date should palpable nodal metastases become evident or after the completion of pregnancy.
12. Follow-up Practice Guidelines

Patients diagnosed with melanoma are followed to detect recurrent disease or additional melanomas. Also, it gives the physician a good opportunity to provide sun safety education, follow other pigmented nevi and answer additional questions patients may have. Visits should emphasize monthly cutaneous and lymph node self-examination. Frequency of follow-up visits is determined by risk of recurrent disease and presence of other risk factors including: history of multiple melanomas, presence of atypical nevi, family history, patient anxiety and patient’s ability to reliably perform self-examination.\textsuperscript{7, 25, 26, 28, 64} The actual follow up does vary somewhat and is provided as a guideline. Obviously, patient factors will dictate the actual follow-up plan.

The chart below suggests intervals for follow up, in the absence of established, evidence-based guidelines for interval frequency. As most relapses occur within the first 5 years, interval follow-up is outlined accordingly.\textsuperscript{64} Risk for delayed relapse should be considered and annual follow up beyond 5 years is discretionary.

For asymptomatic patients, routine surveillance blood work or imaging is not justified given low yield for detection of metastatic disease and high false-positive rates.\textsuperscript{64} Investigations should be guided by findings on history and physical examination.

Patients with thin, primary melanomas may be followed by surgeon, dermatologist, and/or family physician familiar with melanoma care.

Patients with more advanced melanomas, recurrent or node positive disease, distant metastases or other high risk factors would benefit from a multidisciplinary approach that ideally includes a dermatologist, surgeon, oncologist and family physician.

It is important that the patient understand who is responsible for follow up.

NB: \textit{In situ} melanomas, once completely surgically excised, can be followed on a discretionary basis by the patient’s family physician and treating specialist. If the patient has other risk factors as outlined above, consideration should be given to regular follow-up.
<table>
<thead>
<tr>
<th>Stage</th>
<th>Frequency of Follow up Assessments</th>
</tr>
</thead>
</table>
| Stage 1| Every 3-6 months for first 3 years  
|        | Every 6 months until year 5        
|        | Consider annual follow up thereafter |
| Stage 2| Every 3 months for first 3 years   
|        | Every 6 months until year 5        
|        | Consider annual follow up thereafter |
| Stage 3| Every 3 months for first 3 years   
|        | Every 6 months until year 5        
|        | Consider annual follow up thereafter |
| Stage 4| Every 3 months or at discretion of treating physician |
13: Supportive Care Issues

Supportive Care in Melanoma Patients

All cancer patients have a number of supportive care needs, often including the need for psychosocial support. The supportive care needs of individual melanoma patients varies depending on the stage of disease at diagnosis, whether it is a new diagnosis or a recurrence, the difficulty in resection or treatment and risk of disfigurement as a result of treatment. As well, the supportive care needs of an individual will change over the course of the disease.

It is the responsibility of the melanoma health care team to provide basic support through the continuum of disease. Regular whole patient assessment (including screening the patient for distress (see below) should be conducted and the goals of care changed as appropriate. In addition to clinical therapy, psychosocial support after diagnosis and therapy may be needed, especially among patients with poor overall health status, those with certain personality types (e.g. maladaptive coping styles), and those without a social network. Referral to other interdisciplinary team members (such as the psychosocial oncology team at Capital Health) to address issues may be appropriate.

The needs of melanoma patients differ from those of patients with other cancer diagnoses as the majority of melanoma patients will not have life-threatening disease. Survivors of cancers who are treated with less aggressive therapies, have relatively good survival rates and have lived many years with disability may be more concerned about fear of recurrence and less troubled by physical impairments resulting from the cancer itself or its treatment. Not all patients with melanoma exhibit clinical levels of psychological distress or need intensive psychosocial support. Many melanoma patients adjust and cope well. However, it is important that those who require psychosocial and palliative care are identified and provided with necessary supports.

While the survival rate for melanoma is high, the impact of the diagnosis and treatment can have a significant impact. Approximately 30% of melanoma patients experience considerable levels of distress, mostly at the time of diagnosis and following treatment. This is in keeping with other work showing that approximately one-third of cancer patients experience clinically significant depression, anxiety and adjustment difficulties. Many cancer patients, regardless of their diagnosis, experience periods of distress at critical points in the cancer trajectory such as during investigation or at diagnosis, the start and end of treatment as well as at times of recurrence or transition to palliative care.
Psychosocial support may be needed for help in coping with the cancer experience. Formal mental health support may also be needed for a significant minority of patients. Since a cancer diagnosis also impacts a patient’s partner, family and support system, they may also require support. 90

Two recent systematic reviews related to supportive care and melanoma patients have been conducted. One reviewed health-related quality of life (HRQOL) (13 studies written in English published between 2001 and 2008) 88 and the other psychological responses and coping strategies in melanoma patients. 90

Cornish 88 reported high levels of HRQOL impairment following definitive diagnosis as well as during the period of investigation leading to diagnosis. Patients reported more pain, less energy and more interference of physical and emotional stressors on social activities. Importantly, patients also gave worse evaluations of overall personal health at these times. In the follow-up phase, psychological distress can interfere with screening recommendations and preventive behaviours. Female sex, older age, co-morbidities, and advanced tumour stage are all significantly associated with poorer health-related quality of life. 88, 93, 94

Cornish 88 noted that a mal-adaptive coping style was a determinant in the negative impact of melanoma on health-related quality of life and Kasparin 83 found a positive association between active-cognitive coping styles and healthy emotional adjustment to melanoma. Vurnek Zivkovic 95 notes that perceptions of illness explain coping responses and emotional distress caused by the illness and that this does not always correspond to severity of illness.

Comparative studies of patients treated with Interferon and control groups showed that patients on interferon scored significantly lower on their HRQOL than the control group. 88

With regards to scarring, two studies 96, 97 compared the effects of size of excision margins on HRQOL. One study 96 found that patients with larger (3 cm) scars reported lower health-related quality of life scores than those with smaller (1 cm) scars during the immediate post-surgical period but that this difference had largely disappeared by 6 months post-op, although those with the 3 cm scars were more likely to have a persistently poor view of their scar. A second study 97 comparing the impact of narrow (2 cm) and wide (4 cm) excision margins found no differences for HRQOL at any time (3, 9 and 15 months post-op). One-third of patients reported problems with their scar but there was no difference between the 2 arms.

Four studies 93, 94, 95, 99 compared the HRQOL of melanoma survivors with that of the general population and found that their HRQOL is the same or better than that of the general population. A Dutch cross-sectional population
study of 562 melanoma survivors (mean time since diagnosis 4.6 years) found no significant difference compared to age and sex-matched samples from the general Dutch population. A second study compared HRQOL in Dutch melanoma patients (mean 4 years of follow up) who had undergone either axillary or inguinal sentinel lymph node biopsy to each other and to a reference group of the German normal population. The mean scores of the melanoma survivors were statistically significantly higher than those of the healthy norm population. The third study compared 664 melanoma survivors two years after initial therapy with the German general population and found a comparable quality of life. A small study of 60 melanoma patients in Croatia (mean duration of illness 3 years) also found that the average quality of life was the same as that of healthy populations.

The finding that melanoma survivors report HRQOL as good as or better than the general population is in keeping with other studies that have shown that cancer survivors have better HRQOL than the general population, possibly because of a change in perception of health as a result of their cancer experience. Schelesginer-Raab’s study reported that 50% of respondents with localized malignant melanoma reported a change for the better in their attitude towards life two years after treatment.

Practical Support

Cancer patients are frequently challenged by practical issues such as transportation, especially to a tertiary centre, and financial barriers including access to drugs due to lack of insurance coverage. Cancer Patient Navigators may be able to provide assistance for those in need of referrals to other agencies.

Screening for Distress

In Nova Scotia, it is recommended that all people diagnosed with cancer be screened for distress at critical times (such as the start and end of cancer treatment, transition to survivorship or end-of-life care, disease progression or recurrence and other stressful times) throughout the cancer continuum. The formal implementation of screening for distress in cancer patients using a common, standardized tool began in Nova Scotia in 2009 and is currently available to patients in every district health authority (DHA). The service continues to be expanded with the goal that all newly diagnosed cancer patients in Nova Scotia will be offered screening for distress.

The objective of screening for distress is to quickly and briefly identify the patients experiencing distress. Screening allows the health care provider to determine the need for further assessment and referral to healthcare specialists for assessment, management of concerns and treatment. Assessment is a thorough examination of the individual’s concerns, conducted after screening.
Risk factors to consider in selecting the frequency to screen for distress screening include:

- age < 60
- a history of mental illness
- social isolation / limited social supports
- greater burden of illness
- advanced stage of cancer
- post-treatment physical changes / losses
- multiple life stressors

A systematic review of the psychological responses and coping strategies of patients with malignant melanoma found that patients diagnosed as having advanced disease, a deteriorating physical condition, or with tumours located on visible parts of the body, such as the face or hands, have been found to report higher levels of psychological distress. It also found that women, those younger in age and those who are unmarried, with fewer children or with lower levels of education are more likely to report symptoms of psychological distress. Stage of cancer at diagnosis and time since diagnosis were not found to be significant predictors of general distress in melanoma patients.

Managing Distress

Referral pathways have been developed to assist health professionals in Nova Scotia address concerns raised through distress screening that are beyond the abilities of the front-line caregivers. These pathways will be available in the Cancer Care Nova Scotia Best Practice Guideline for the Management of Cancer-related Distress in Adults (expected in early 2014).

Structured interventions offering psycho-educational support can reduce distress and mood disturbances and lead to greater use of active coping strategies among individuals affected by melanoma.

Approaches for the ongoing management of psychosocial and emotional difficulties include the following:

- Encouraging patients to use their constructive coping/stress management strategies
- Providing patients with information and education on their disease and treatment
- Helping patients access positive social supports.
- Encouraging patients to focus on a whole-person approach to coping with their illness (i.e., physical, psychological, social, spiritual).
- Encouraging patient involvement in relevant support groups, if appropriate.
- Referring patients to psychosocial oncology healthcare professionals (i.e., psychologists, psychiatrists, social workers, spiritual care workers, advanced practice nurses) for consultation and treatment (e.g., psychoeducation, counseling, and psychotherapy, as appropriate). There are psychosocial oncology resources available through the Capital Health Cancer Care
Program (902-473-5140) and the Cape Breton Cancer Centre (902-567-7771) for patients registered with these programs.

Cancer Patient Navigators are a valuable resource for patients and families and are available in every Nova Scotia District Health Authority except Capital Health. See below for contact information.

For more information about screening for distress and providing psychosocial support to melanoma and other cancer patients, please see:

- The Pan-Canadian Practice Guideline: Screening, Assessment and Care of Psychosocial Distress (Depression, Anxiety) in Adults with Cancer [www.capo.ca](http://www.capo.ca)
- Best Practice Guidelines for the Management of Cancer-Related Distress in Adults [92]

**Resources for Patients**

Schlesinger-Raab [93] found that patients who reported good communication with their health care team had significantly better emotional and social functioning, better body image and less worry about the future. However, 53% of respondents did not receive as much information as they would have liked. One cross-sectional study [89] found that patients who are recently diagnosed with malignant melanoma need information about the diagnosis and treatment, life expectancy and the likely effect on work and family life.

There are a number of local and national resources for melanoma patients living in Nova Scotia:

- Cancer Care Nova Scotia, in partnership with the Canadian Cancer Society-Nova Scotia Division, maintains an Inventory of Psychosocial Resources in Nova Scotia for health care professionals, who care for cancer patients, to assist them and individuals affected by cancer in more readily accessing psychosocial services when needed. The inventory includes a list of both public and private psychosocial resources, available in each of the nine health districts. The focus is on licensed health care professionals, who provide psychosocial and supportive care to patients. The inventory can be accessed at [www.cancercare.ns.ca/psychosocialinventory](http://www.cancercare.ns.ca/psychosocialinventory)
- The Canadian Cancer Society's Information Service (1 888 939-3333 [www.cancer.ca](http://www.cancer.ca)) can connect patients and families to peer support, local resources and additional sources of information including materials in languages other than English.
- There are a number of patient information sheets on a wide variety of topics related to aspects of cancer care including financial issues, accessing psychosocial support, side effects and symptom management.
on the Cancer Care Nova Scotia website (www.cancercare.ns.ca Patients and Families, Cancer Information)

- The Emotional Facts of Life with Cancer is a guide to counseling and support for patients, family members and friends. It is available at www.capo.ca (Resources, Professional and Student Info).
- Young Adult Cancer Canada (www.youngadultcancer.ca) provides information and support to young adults living with any cancer diagnosis.

**Pain and Symptom Management**

A number of resources exist for patients who need help with pain or symptom management and/or palliative care. These include the attending oncology team, the Cancer Patient Navigator, and the local palliative care team and the CCNS Supportive Care guidelines.

Some patients may need access to prosthetic and lymphedema services.\(^8^9\) The Cancer Patient Navigators and the Canadian Cancer Society Information Service can assist with finding these services close to patients’ homes.

Only a small proportion of melanoma cancer patients require specialist palliative care. However, it is very important to ensure that these patients get referred.\(^8^9\)
## Contact Information for District Supportive Cancer Care and Palliative Care Services:

<table>
<thead>
<tr>
<th></th>
<th>Cancer Patient Navigator</th>
<th>Palliative Care</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>South Shore Health</strong></td>
<td>(902) 527-5820</td>
<td>902-634-7369 or 902-354-3436</td>
</tr>
<tr>
<td><strong>South West Health</strong></td>
<td>(902) 749-1523</td>
<td>902-742-3542 ext 414</td>
</tr>
<tr>
<td><strong>Annapolis Valley Health</strong></td>
<td>(902) 690-3700</td>
<td>902-678-7381 ext 2270</td>
</tr>
<tr>
<td><strong>Colchester East Hants Health Authority</strong></td>
<td>(902) 893-2549</td>
<td>902-893-5554 ext 2306</td>
</tr>
<tr>
<td><strong>Cumberland Health Authority</strong></td>
<td>(902) 667-6424</td>
<td>902-667-5400 ext 6373</td>
</tr>
<tr>
<td><strong>Pictou County Health Authority</strong></td>
<td>(902) 752-7600 ext 4922</td>
<td>902-752-7600 ext 4190</td>
</tr>
<tr>
<td><strong>Guysborough Antigonish Strait Health Authority</strong> (includes Richmond and part of Inverness Counties)</td>
<td>(902) 867-4500 ext 4707</td>
<td>902-867-4296 or 902-867-4436</td>
</tr>
</tbody>
</table>

**Cape Breton District Health Authority**

<table>
<thead>
<tr>
<th>Victoria County</th>
<th>Cancer Centre Psychosocial Team</th>
<th>Palliative Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>902-336-2504</td>
<td>902-473-5140</td>
<td>902-473-3119</td>
</tr>
<tr>
<td>902-295-2112</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inverness County</td>
<td></td>
<td></td>
</tr>
<tr>
<td>902-224-4002</td>
<td></td>
<td></td>
</tr>
<tr>
<td>902-258-1129</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cape Breton County</td>
<td>902-567-7122</td>
<td>902-567-7846</td>
</tr>
</tbody>
</table>

## Contact Information for Cancer Centre Supportive Cancer Care and Palliative Care Services:

<table>
<thead>
<tr>
<th></th>
<th>Cancer Centre Psychosocial Team</th>
<th>Palliative Care</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Capital Health Cancer Care Program</strong></td>
<td>902-473-5140</td>
<td>902-473-3119</td>
</tr>
<tr>
<td><strong>Cape Breton Cancer Centre</strong></td>
<td>902-567-7771</td>
<td>902-567-7846</td>
</tr>
</tbody>
</table>
Other Related CCNS guidelines

Guidelines for the management of distress are under development by the CCNS Supportive Care Cancer Site Team. When this guideline is completed, it will be posted on the Cancer Care Nova Scotia website (www.cancercare.ns.ca).

CCNS symptom management guidelines include:
• Management of Nausea & Vomiting (2004)
• Management of Cancer-Related Pain (2006)
• Management of Oral Complications from Cancer Therapy (2006)
14. Referral Process

Referral Process:
Delay, misdiagnosis or mismanagement of malignant melanoma can have a negative effect on patients' chances of survival. Therefore these patients need to be urgently referred to and managed by a hospital-based multidisciplinary team with specialist skills.89

Referral for Suspicious Lesions and/or Malignant Melanoma

Patients who present with suspicious new lesions or changes in existing lesions should be referred for biopsy and definitive care to a dermatologist or surgeon with experience in melanoma. Suspicious lesions include those with the ABCDE (A)symmetry, (B)order irregularity, (C)olor variegation, (D)iameter greater than 6 mm, (E)volving or changing).

The development of any symptoms (itching) or signs (enlargement, asymmetry, darkening, bleeding, ulceration) should prompt referral for assessment of a pigmented lesion.

Patients may be referred either for biopsy or for consultation after the pathology report from the biopsy is received.
Referral

The following information should accompany the referral. **Referrals should not be delayed pending tests or reports. Send the referral while awaiting results to facilitate a timely appointment for your patient.** The date and location of the procedure should be noted so that results can be obtained when available.

- Patient information
  - Date of birth
  - Address
  - Telephone number(s)
  - Health Card number
- Biopsy results (if known)
- Lab Results (if known)
- Imaging Reports and Films (where appropriate)
- Operative Reports relevant to the melanoma (where appropriate)
- Past history
- Any other cancers

**Residents of mainland Nova Scotia**
(except residents of Guysborough and Antigonish counties)

New consultation requests for newly diagnosed melanoma patients requiring wide excision and sentinel lymph node biopsy or patients with suspicious skin lesions requiring biopsy can be sent to the:

**Melanoma Clinic**: fax 902-473-8773 (tel. 902-473-7054)

Referrals to **Medical Oncology** or **Radiation Oncology** of pathologically confirmed malignant melanoma can be faxed to:

The Nova Scotia Cancer Centre Referral Office at **902-473-6079** fax (tel. 902-473-5140).

A letter of referral and a pathology report documenting the cancer diagnosis are the usual minimal requirements although it is preferred that referrals be accompanied by the Cancer Care Program (CCP) Referral form available upon request at the above phone numbers or available for downloading at [www.cdha.nshealth.ca/physicians/documents](http://www.cdha.nshealth.ca/physicians/documents) (choose forms).

For urgent or emergent referrals, please page the appropriate specialist on call through the QEII HSC Locating service (902-473-2220) to discuss the referral.
For Residents of Cape Breton Island and Guysborough and Antigonish counties

Referrals to Medical Oncology or Radiation Oncology of pathologically confirmed malignant melanoma can be faxed to:

The Cape Breton Cancer Centre at **902-567-7911fax** (tel. 902-567-7227)

For urgent or emergent referrals, please page the appropriate specialist on call through the Cape Breton Regional Hospital Locating service (902-444-4444) to discuss the referral.

**Pediatric Melanoma**

Pediatric cancers are specifically **not** covered within this guideline. For pediatric and adolescent patients, referral calls to the IWK Health Centre may be directed to the pediatric hematologist/oncologist or pediatric plastic surgeon on call at 902-470-8888.

Surgical biopsy or other intervention is **not** recommended until initial contact has been made with the IWK Health Centre pediatric plastic surgeon. Further diagnostic investigations will be determined after initial contact and discussion.

The following information is needed for a telephone consultation: name and age of the patient, parent’s name and phone number, relevant history and physical examination, presumptive diagnosis, and any initial investigation results. This information can also be faxed to 902-470-7208.
APPENDIX I Resection Margins

In the past, considerable controversy has surrounded the choice of resection margins in melanoma. Recent prospective, randomized surgical trials are now providing evidence to guide surgical management of melanoma.

The WHO prospective, randomized study comparing 1 vs. 3 cm margins has, for melanomas < 1.0 millimeter thick, confirmed the efficacy and safety of 1.0 cm margins. The Intergroup Melanoma Study demonstrated in a prospective, randomized trial for melanomas of intermediate thickness (1.5 – 4 mm) that there was no significant difference in survival or local recurrence when comparing 2 cm vs. 4 cm margins.

A recent UK melanoma study group trial randomized patients with melanomas >2.0 mm to 3.0 mm thick with no significant difference in survival or local recurrence, but increased local-regional recurrence in the group with 1 cm margins. The study data do not support margins of 2 cm vs. 3 cm, but argue against a margin of 1 cm for melanomas of 2-4 mm thick.

Most evidence supports a margin of 1 to 2 cm for lesions < 2 mm taking issues of cosmesis, location, and functionality and wound closure into consideration. For thick melanomas (> 4 mm) the guidelines are less certain because no prospectively randomized study has specifically addressed the issue of excision margins for these lesions. Based on currently available data it is unlikely that margins exceeding 2 cm significantly impact on the higher rates of local recurrence (12%) and poor survival (55% at 5 years) with which these lesions are associated. If the melanoma is in proximity to a vital organ or when wider margins entail a more complicated procedure, lesser margins are often utilized.
Appendix II: Lymphatic Mapping/Sentinel Lymph Node Biopsy (SLNBx)

- Pre-operative lymphoscintography (technetium antimony sulfur colloid) identifies nodal basins, sentinel nodes
- Intra-operative mapping
  - Facilitates minimally invasive surgery
    Patent blue or methylene blue dye
  - Technetium-99 with gamma probe localization
  - Permanent sections: if positive, completion lymph node dissection

Appendix III: Primary Invasive Malignant Melanoma  
(Surgical Pathology Report template)

Microscopic Description:

The malignant melanoma in this specimen has the parameters itemized below.

Breslow thickness:
Clark Level:
Ulceration:
Mitotic Rate*:
*(Note: melanomas ≤1mm in thickness only: <1 mitosis/mm² or ≥1 mitosis/mm²)
Microsatellitosis:
Peripheral Margins:
Deep Margin:
Other special features:

Diagnosis:

SKIN (ANATOMIC SITE), PROCEDURE:
- MALIGNANT MELANOMA, (pathologic stage)
- MARGIN STATUS

Pathologic Staging [AJCC 7th edition TNM Staging System] Key:

Primary Tumor (pT)
pT1a: Melanoma 1.0 mm or less in thickness, no ulceration, <1 mitoses/mm²
pT1b: Melanoma 1.0 mm or less in thickness with ulceration and/or 1 or more mitoses/mm²
pT2a: Melanoma 1.01 to 2.0 mm in thickness, no ulceration
pT2b: Melanoma 1.01 to 2.0 mm in thickness, with ulceration
pT3a: Melanoma 2.01 to 4.0 mm in thickness, no ulceration
pT3b: Melanoma 2.01 to 4.0 mm in thickness, with ulceration
pT4a: Melanoma greater than 4.0 mm in thickness, no ulceration
pT4b: Melanoma greater than 4.0 mm in thickness, with ulceration

***When microsatellitosis is identified***
pN2c: Satellite or in-transit metastasis without nodal metastasis
### Appendix IV Benign Lesions that May Mimic Skin Cancer

<table>
<thead>
<tr>
<th>Lesion Type</th>
<th>Clinical Characteristics</th>
<th>How to Differentiate from Skin Cancer</th>
<th>Example</th>
</tr>
</thead>
</table>
| Seborrheic Keratosis         | Papules or plaques, with or without pigment, that may have a “stuck-on” or greasy appearance or feel; Small, white keratin cysts (horn cysts) may be visible with close examination or dermoscopy | ° Presence of horn-cysts  
° May be easily removed from the underlying skin by shave biopsy | ![Image](image1.jpg) |
| Dermatofibroma                | Solitary, firm, well-defined papular or nodular lesions usually found on the trunk or extremities, brown/ red in color | ° Presence of “retraction sign”; lesion dimples when surrounding skin is compressed | ![Image](image2.jpg) |
| Sebaceous Hyperplasia        | Small, soft, skin-colored papules (1-3 mm in diameter) with central umbilication; ** May have telangiectasia and are often mistaken for basal cell carcinomas | ° Central punctum  
° Sebum may be released on compression | ![Image](image3.jpg) |
| Solar Lentigo                 | Well-defined tan to brown macule, commonly 1-3cm in diameter; variable in color and shape and appear exclusively on sun-exposed areas; More common in individuals over 40 years of age with skin | ° Can be differentiated from lentigo maligna based on evaluation of the “ABCDs”  
° Suspicious lesions should be biopsied to confirm the diagnosis | ![Image](image4.jpg) |
| Verruca Vulgaris (Common Wart)| Firm papules, 1-10 mm in diameter with a hyperkeratotic or clefted surface | ° Presence of back “dots” – thrombosed vessels within the lesion | ![Image](image5.jpg) |
| Keratoacanthoma              | Smooth, red papule that grows rapidly over a number of weeks, after which the tumor resembles a crater filled with keratin; often found in conjunction with actinic keratosis; More common in light-skinned | ° Can be differentiated based on characteristic clinical appearance  
° Suspicious lesions should be biopsied to confirm the diagnosis | ![Image](image6.jpg) |
<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
<th>Can be differentiated based on characteristic clinical appearance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyogenic Granuloma</td>
<td>Smooth, bright red, violaceous or brown-black papule caused by overgrowth of capillaries</td>
<td>on characteristic clinical appearance</td>
</tr>
<tr>
<td></td>
<td>Usually develops rapidly following minor trauma</td>
<td></td>
</tr>
<tr>
<td>Keloid</td>
<td>Firm, tender, well-defined nodule or plaque; atypically large scar resulting from the abnormal growth of fibrous tissue</td>
<td>on characteristic clinical appearance</td>
</tr>
<tr>
<td></td>
<td>Common in young adults and in dark skinned individuals</td>
<td></td>
</tr>
<tr>
<td>Skin Tag (acrochordon)</td>
<td>Soft, skin-colored papule or flap, typically occurring on the axillae or neck.; may appear smooth and flat, folded or pedunculated.</td>
<td>on characteristic clinical appearance</td>
</tr>
<tr>
<td>Halo Nevus</td>
<td>Brown, papular, junctional, compound, or dermal nevus encircled by an area of depigmentation.</td>
<td>Can be differentiated from melanoma based on evaluation of the “ABCDEs”</td>
</tr>
<tr>
<td></td>
<td>Suspicious lesions should be biopsied to confirm the diagnosis</td>
<td></td>
</tr>
<tr>
<td>Blue Nevus</td>
<td>Firm, well-defined, dark-blue to gray-black papules or nodules; usually &lt; 10 mm in diameter and round to oval in shape</td>
<td>Lesion are typically congenital with no history of change</td>
</tr>
<tr>
<td></td>
<td>Suspicious lesions should be biopsied to confirm the diagnosis</td>
<td></td>
</tr>
<tr>
<td>Nevus Spilus</td>
<td>Oval or irregularly-shaped, lightly-pigmented flat lesion containing focal areas of dark brown hyperpigmented macules or papules</td>
<td>Can be differentiated based on characteristic clinical appearance</td>
</tr>
<tr>
<td></td>
<td>Rate of malignant transformation is very low</td>
<td></td>
</tr>
</tbody>
</table>
Appendix V. Basic Skin Cancer Treatment Algorithm

Legend

Yes ➔ No ➔

Act

Patients that are “high risk” and do not have a plan for monitoring established by a dermatologist.

Reassure

Lesions that meet clinical criteria for benign lesions typical of:
- seborrheic keratosis
- dermatofibroma
- dermal nevus
- cherry angioma
- freckle/lentigo/cale-au-lait spot

Act

Reassure

Lesions that have been present for less that 3 weeks unless the history is deemed unreliable.

Act

Reassure (But reevaluate if not gone in a month)

Lesions that are:
- eroded, ulcerated, bleeding, or encrusted > 3 weeks
- translucent papules with telangiectasia
- keratotic lesions on the face, ears, lips, or genitalia that are not typical seborrheic keratoses

Act

Reassure

Lesions that are less than 3mm, absolutely flat, and no change by observation or history.

Act

Reassure

Lesions that are:
- asymmetrical
- irregularly bordered
- multicolored or irregularly pigmented
- changing in size, shape, surface, or color

Act

Reassure

Lesions that are black on people whose non-sun exposed skin is white or light tan.

Act

Reassure

Small (< 6mm) lesions if they have not changed historically or by observation (and not satisfied any of the above criteria for ‘act’).

Track
Appendix VI Guideline Development Process

This guideline was written by members of the Cancer Care Nova Scotia Melanoma Cancer Site Team (CST), headed by Dr. Carman Giacomantonio until 2009 and then by Dr Steven Morris and supported by Jill Petrella of Cancer Care Nova Scotia (initial work done by Brenda Sabo). The Cancer Care Nova Scotia (CCNS) Guideline Resource Team advised on process and format issues. Members of the Melanoma CST completed a Statement of Conflict of Interest.

This guideline was written for an audience of general practitioners and other non-oncology specialist health professionals involved in caring for patients with melanoma. As such, it is a synthesis of knowledge and evidence, and reflects the practice policies of the Melanoma Cancer Site Team in Nova Scotia.

The guideline was developed through informal consensus in 2005 and 2006 with the external review conducted in fall 2006. In keeping with CCNS normal practice, two versions of the guideline were developed – the “Full” version with explanation and evidence supporting the recommendations and the “Quick Reference Version” which is primarily the graphic flowcharts and other summarized information. Once the draft documents were finalized by the CST, they were distributed to a group of community reviewers along with a standardized questionnaire in fall 2006. The purpose of the review was to ensure that the recommendations in the guidelines were acceptable as well as that the guideline format met users’ needs.

The Full Guideline was sent to:
- all general surgeons in Nova Scotia
- all dermatologists in Nova Scotia and New Brunswick
- all Directors of Anatomic Pathology in Atlantic Canada
- Medical and Radiation Oncologists in Atlantic Canada
- Directors of Hospital Pharmacy in Atlantic Canada

The Quick Reference Guideline was sent to:
- Cancer Patient Navigators in Nova Scotia
- Nurse Managers of Day Surgery Clinics in Nova Scotia
- Nurse Practitioners in Nova Scotia
- Family Physicians who have expressed willingness to review draft CCNS guidelines
- Radiation Therapists in Nova Scotia
- Oncology Nurses in Nova Scotia

There was no reminder to non-respondents. All responses were anonymous. 199 surveys were sent out with 34 returns: 9 respondents reviewed the Full Version, 24 respondents reviewed the QRV and 1 respondent reviewed both.

An overall return rate could not be calculated because groups such as Radiation Therapists and nurses were offered the opportunity to respond through
their managers and we do not know how many individuals were given the opportunity to respond. Results are presented on the next page.

Due to unforeseen circumstances, we were unable to finalize the guideline in 2007. In 2011, the team reviewed the 2006 draft, the feedback from the external review and updated the guideline as needed.

As part of the updating process in 2011, a search was conducted for melanoma guidelines developed in other jurisdictions using the National Guideline Clearinghouse and the SAGE databases as well as the websites of known guideline developers and all Canadian provincial cancer agency (or equivalent) websites. The Nova Scotia recommendations were compared to the recommendations from these guidelines and discrepancies were flagged for discussion by the team.

For the supportive care section, a review of the literature was conducted in PubMed. As two systematic reviews published in 2009 were found, further review was limited to articles published in English from 2006 to September 2011. The reference lists of all publications identified were examined for relevant articles not captured by the initial literature search.

Search strings included:


"psychology"[Subheading] AND ("melanoma"[MeSH Terms] OR "melanoma"[All Fields]) AND ("skin"[MeSH Terms] OR "skin"[All Fields])) NOT non-melanoma[All Fields] AND English[lang]

Concurrently with the development of the Melanoma guideline, an educational booklet for all skin cancers (Skin Cancer: An Overview of Non-melanoma Cancers and Melanoma) was developed for primary care providers in Nova Scotia. Effort was made to ensure the melanoma content in the booklet reflected the recommendations in the guideline. It was decided that this booklet would serve as the Quick Reference Version of the Melanoma guideline.

The revised 2011 draft was reviewed and approved by the Melanoma Cancer Site Team in 2013. The CST-approved document was reviewed by the Guidelines Resource Team against the AGREE tool for guideline evaluation. The final guideline was approved by the Chief Medical Director for Cancer Care Nova Scotia and the Nova Scotia Department of Health and Wellness.

The guideline will be reviewed three years after approval or revised as new evidence becomes available.

The development of this guideline was funded by CCNS. CCNS staff also support the guideline development process and conducted the external review. CCNS
funded the design, printing, and dissemination of the external review as well as the printing and dissemination of the approved guideline. The views and interests of CCNS have not influenced the Melanoma CST’s recommendations in this guideline.

The full version will be circulated to the cancer chemotherapy clinics, Cancer Patient Navigators, Radiation Therapy areas, Day Surgery Clinics, regional hospital pharmacies and surgeons, dermatologists and other physicians involved in the treatment of melanoma in Nova Scotia and posted on the CCNS website.

Please contact Cancer Care Nova Scotia (CCNS) at 1-866-599-2267 or download from the CCNS website (www.cancercare.ns.ca).
Survey Results

<table>
<thead>
<tr>
<th></th>
<th>NS</th>
<th>NB</th>
<th>PEI</th>
<th>NL</th>
<th>Total</th>
<th>Responses</th>
<th>Percent response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathology</td>
<td>10</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>14</td>
<td>1</td>
<td>7.14</td>
</tr>
<tr>
<td>Dermatology</td>
<td>10</td>
<td>9</td>
<td></td>
<td></td>
<td>19</td>
<td>3</td>
<td>15.79</td>
</tr>
<tr>
<td>Family Physician</td>
<td>28</td>
<td></td>
<td></td>
<td></td>
<td>28</td>
<td>7</td>
<td>25</td>
</tr>
<tr>
<td>General Surgeon</td>
<td>35</td>
<td></td>
<td></td>
<td></td>
<td>35</td>
<td>4</td>
<td>11.43</td>
</tr>
<tr>
<td>Medical Oncology</td>
<td>4</td>
<td>7</td>
<td>2</td>
<td>2</td>
<td>15</td>
<td>1</td>
<td>6.67</td>
</tr>
<tr>
<td>Oncology Nurses</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Day Surgery Nurses</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Nurse Practitioners</td>
<td>14</td>
<td>1</td>
<td></td>
<td></td>
<td>15</td>
<td>1</td>
<td>6.67</td>
</tr>
<tr>
<td>Cancer patient Navigators</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td>5</td>
<td>2</td>
<td>40</td>
</tr>
<tr>
<td>Hospital Pharmacists</td>
<td>18</td>
<td>7</td>
<td>2</td>
<td>10</td>
<td>37</td>
<td>3</td>
<td>7.89</td>
</tr>
<tr>
<td>Radiation Oncologists</td>
<td>3</td>
<td>9</td>
<td>1</td>
<td>1</td>
<td>14</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Radiation Therapists</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Totals</td>
<td>131</td>
<td>34</td>
<td>7</td>
<td>14</td>
<td>186</td>
<td>42</td>
<td></td>
</tr>
</tbody>
</table>
Key Questions:

1. Overall, you agree with the content and recommendations of the guideline

<table>
<thead>
<tr>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Neither Agree nor Disagree</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
<th>Unanswered</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>15</td>
<td>2</td>
<td></td>
<td></td>
<td>11</td>
</tr>
</tbody>
</table>

2. A guideline on this topic will be useful to clinicians?

<table>
<thead>
<tr>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Neither Agree nor Disagree</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
<th>Unanswered</th>
</tr>
</thead>
<tbody>
<tr>
<td>14</td>
<td>16</td>
<td>1</td>
<td></td>
<td></td>
<td>3</td>
</tr>
</tbody>
</table>

3. Would you use this guideline in your own practice?

Yes 25  
No 1  
Unsure 7  
Unanswered 1

4. The format of the guideline is easy to use

<table>
<thead>
<tr>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Neither Agree nor Disagree</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
<th>Unanswered</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>21</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
5. Should the guideline be disseminated to appropriate health care practitioners?

<table>
<thead>
<tr>
<th>Should the guideline be disseminated to appropriate health care practitioners?</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Once it is approved, and periodically afterwards as new versions are approved</td>
<td>24</td>
</tr>
<tr>
<td>Only in response to a patient referral for specialist care (e.g. to a cancer centre)</td>
<td>2</td>
</tr>
<tr>
<td>Practitioners should be notified when it is available on the website, and they can get it themselves as they choose</td>
<td>15</td>
</tr>
<tr>
<td>Other</td>
<td>?mailed with path report - Dx melanoma</td>
</tr>
<tr>
<td>Unanswered</td>
<td>3</td>
</tr>
</tbody>
</table>

Most feedback was of an editorial nature (spellings, cross-references etc). The most significant feedback regarding content was about the appropriate use of Sentinel Lymph Node Dissections and Interferon α2B. These sections were re-written based on feedback received.
References


91. Howell, D., Keller-Olaman, S., Oliver, T., Hack, T., Broadfield, L., Biggs, K., ... Syme, A. (2010). *A Pan-Canadian Practice Guideline: Screening, Assessment and Care of Psychosocial Distress (Depression, Anxiety) in Adults with Cancer*. Toronto: Canadian Partnership Against Cancer (Cancer Journey Action Group) and the Canadian Association of Psychosocial Oncology.


**Melanoma Site Team Members**  
(2001-2013)

The following is a list of members of the Melanoma Cancer Site Team from 2001-2013 and who have contributed in some way to the writing of this guideline. A list of current members can be obtained by contacting Cancer Care Nova Scotia.

<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slawa Cwajna</td>
<td>Radiation Oncologist, CDHA</td>
</tr>
<tr>
<td>Mary Davis</td>
<td>Medical Oncologist, CDHA</td>
</tr>
<tr>
<td>Carman Giacomantonio</td>
<td>Surgical Oncologist, CDHA</td>
</tr>
<tr>
<td>(Chair 2001-2008)</td>
<td></td>
</tr>
<tr>
<td>Jill Flinn</td>
<td>Manager, Nova Scotia Cancer Centre, CDHA</td>
</tr>
<tr>
<td>Peter Green</td>
<td>Dermatologist, CDHA</td>
</tr>
<tr>
<td>Rob Hart</td>
<td>Head and Neck Surgeon, CDHA</td>
</tr>
<tr>
<td>Lucy Helyer</td>
<td>Surgical Oncologist, CDHA</td>
</tr>
<tr>
<td>Richard Langley</td>
<td>Dermatologist, CDHA</td>
</tr>
<tr>
<td>Robyn Macfarlane</td>
<td>Medical Oncologist, CDHA</td>
</tr>
<tr>
<td>Heather MacKenzie</td>
<td>CST Administrative Support, CCNS</td>
</tr>
<tr>
<td>Justin Paletz</td>
<td>Plastic Surgeon, CDHA</td>
</tr>
<tr>
<td>Winston Parkhill (retired)</td>
<td>Plastic Surgeon, CHDA</td>
</tr>
<tr>
<td>Jill Petrella</td>
<td>Manager, Quality, CCNS</td>
</tr>
<tr>
<td>Geoff Porter</td>
<td>General Surgeon, CDHA</td>
</tr>
<tr>
<td>Judith Purcell</td>
<td>Prevention Coordinator, CCNS</td>
</tr>
<tr>
<td>Steven Morris (Chair 2008-present)</td>
<td>Plastic Surgeon, CDHA</td>
</tr>
<tr>
<td>Noreen Walsh</td>
<td>Pathologist, CDHA</td>
</tr>
<tr>
<td>Jason Williams</td>
<td>Plastic Surgeon, CDHA</td>
</tr>
</tbody>
</table>