

# Melanoma: Cutaneous, Version 2.2026

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## Abstract

The NCCN Guidelines for Melanoma: Cutaneous provide strategies for the diagnosis, treatment, and follow-up of patients with cutaneous melanoma, which is among the most common cancers in the United States. The outcome of cutaneous melanoma is significantly influenced by stage at initial presentation. Generally, localized disease and smaller primary tumors have been associated with more favorable prognosis. Thus, the select content featured in this issue focuses on risk factors associated with cutaneous melanoma development and which should be considered during an initial assessment. These include (1) phenotypic predispositions, (2) personal medical history or comorbidities, (3) genetic predispositions, and (4) environmental factors.

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## Overview

In 2026, an estimated 112,000 patients will be diagnosed with cutaneous melanoma and about 8,510 patients will die of disease in the United States.<sup>1</sup> Although melanoma incidence has steadily increased over the past several decades, this has largely been due to the diagnoses of melanomas in situ and early stage (T1) melanomas, raising concerns for potential histopathologic overinterpretation.<sup>2</sup> However, data have shown that the thickest (T4) melanomas continue to rise in incidence, particularly in individuals with lower socioeconomic status and/or skin of color.<sup>2</sup> Risk factors for melanoma include individuals assigned male at birth (AMAB), older age (typically >50 years), phenotypic and genetic predisposition, and personal medical history, comorbidities, and environmental factors (see “Risk Factors for Development of Single or Multiple Primary Melanomas,” Figure 1).<sup>1,3–27</sup> Melanoma occurs most often in non-Hispanic White individuals with lighter skin tones but can occur in people with darker skin tones from any racial or ethnic group, and in areas of the body without substantial sun exposure (eg, palms, soles, nails).

As with nearly all malignancies, the outcome of cutaneous melanoma depends on the stage at presentation.<sup>28</sup> In general,

the prognosis is excellent for patients who present with localized disease and primary tumors ≤1.0 mm in thickness, with 5- and 10-year disease-specific survival (DSS) achieved in >96% of patients.<sup>28</sup> For patients with localized melanomas >1.0 mm in thickness, 5- and 10-year DSS range from 75% to 94%, depending on tumor thickness, ulceration, and mitotic rate.<sup>28</sup> When regional nodes are involved, 5- and 10-year DSS range between 24% and 93%, depending on the extent of nodal involvement, although these survival rates exclude data following the use of novel targeted and immune therapies. Patients with clinically occult nodal disease (detected via sentinel lymph node biopsy) generally have better survival than those with clinically evident nodal disease.<sup>28–30</sup> Historically, long-term survival in patients with distant metastatic melanoma was <10% at 5 years, with median survival <1 year.<sup>31–34</sup> However, beginning in the early 2010s, effective systemic therapies for patients with unresectable stage III and stage IV melanoma made long-term remission possible for approximately 50% of patients, and these agents are increasingly being used in the adjuvant setting to prevent disease relapse and improve survival.<sup>35</sup>

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The full NCCN Guidelines for Melanoma: Cutaneous are not printed in this issue of JNCCN. The complete and most recent version of these guidelines is available free of charge at [NCCN.org](https://www.nccn.org).

**NCCN CATEGORIES OF EVIDENCE AND CONSENSUS**

**Category 1:** Based upon high-level evidence ( $\geq 1$  randomized phase 3 trials or high-quality, robust meta-analyses), there is uniform NCCN consensus ( $\geq 85\%$  support of the Panel) that the intervention is appropriate.

**Category 2A:** Based upon lower-level evidence, there is uniform NCCN consensus ( $\geq 85\%$  support of the Panel) that the intervention is appropriate.

**Category 2B:** Based upon lower-level evidence, there is NCCN consensus ( $\geq 50\%$ , but  $< 85\%$  support of the Panel) that the intervention is appropriate.

**Category 3:** Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

**All recommendations are category 2A unless otherwise indicated.**

**NCCN recognizes the importance of clinical trials and encourages participation when applicable and available. Trials should be designed to maximize inclusiveness and broad representative enrollment.**

**PLEASE NOTE**

The NCCN Guidelines<sup>®</sup> are a statement of evidence and consensus of the authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult the NCCN Guidelines<sup>®</sup> is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network<sup>®</sup> (NCCN<sup>®</sup>) makes no representations or warranties of any kind regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

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**Preferred intervention:** Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.

**Other:** Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes.

**Useful in certain:** Other interventions that may be used for selected patient populations (defined with recommendation).

**All recommendations are considered appropriate.**

The currently described clinical subtypes of cutaneous melanoma are low cumulative sun damage (CSD; low-CSD, typically superficial spreading or nodular subtypes), high CSD (typically lentigo maligna subtype, signified by the presence of marked solar elastosis and lentigo maligna growth pattern histologically), and acral melanoma on the soles, palms, or subungual sites. Melanocytes outside the skin can give rise to noncutaneous melanomas on mucosal membranes (eg, in the head and neck sinuses and oral cavity, anorectum, vulva, vagina, and

gastrointestinal and urogenital tracts) and the uveal tract of the eye, or leptomeninges.<sup>36,37</sup> Mucosal and uveal melanomas differ significantly from cutaneous melanoma in presentation, genetic profile, staging, response to treatment, and patterns of progression, and should be treated as diseases distinct from cutaneous melanoma (see NCCN Guidelines for Head and Neck Cancers, NCCN Guidelines for Melanoma: Uveal, and NCCN Guidelines for Vulvar Cancer, available at NCCN.org).<sup>38–41</sup>

**RISK FACTORS FOR DEVELOPMENT OF SINGLE OR MULTIPLE PRIMARY MELANOMAS<sup>a</sup>**

- Male sex<sup>1</sup>
- Age  $> 50$  years<sup>1</sup>
- Phenotypic predisposition
  - ▶ Atypical moles/dysplastic nevi<sup>2</sup>
  - ▶ Increased mole count (particularly large nevi)<sup>3</sup>
  - ▶ Sun phenotype/tendency to sunburn<sup>3</sup>
  - ▶ Red hair-blue eyes/Fitzpatrick skin type I/pheomelanin-predominant phenotype<sup>3</sup>
- Personal medical history/comorbidities
  - ▶ Multiple and/or blistering sunburns<sup>3,4</sup>
  - ▶ Precancer/cancers, especially:
    - ◊ Actinic keratosis/non-melanoma (keratinocyte) skin cancer (eg, basal cell and squamous cell carcinomas)<sup>3</sup>
    - ◊ Childhood cancer<sup>5</sup>
  - ▶ Immunosuppression/immune perturbation related to:
    - ◊ Solid organ transplantation<sup>3,6,7</sup>
    - ◊ Hematopoietic cell transplantation (HCT)<sup>7</sup>
    - ◊ Human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS)<sup>8</sup>
    - ◊ Hematologic malignancies<sup>9,10</sup>
  - ▶ Rare genodermatoses
    - ◊ Xeroderma pigmentosum<sup>11</sup>
- Genetic predisposition
  - ▶ Risk factors: presence of germline pathogenic variants (PV) or polymorphisms predisposing to familial melanoma (eg, *CDKN2A*, *CDK4*, *MC1R*, *BAP1* [especially for uveal melanoma], *TERT*, *POT1*, *MITF*) and other cancer predisposition genes with increased melanoma risk (eg, *TP53*, *PTEN*, *CHEK2*, *BRCA1/2*, *BLM*, *ATM*).<sup>3,12–16</sup>
  - ▶ Consideration of testing and follow-up: family or personal history of  $\geq 2$  invasive cutaneous melanomas; family or personal history of  $\geq 2$  noncutaneous cancers in a patient with melanoma, (especially pancreatic, kidney, GI, and/or breast cancer; with  $\geq 1$  in a first-degree relative), to assess for cancer syndromes that include melanoma.
    - ◊ Patients with a known high-risk PV in the family (especially *CDKN2A*, *BAP1* or *CDK4*) should receive genetic counseling for consideration of germline testing. If the high-risk variant is identified, consider regular skin examination, even in the absence of a personal history of melanoma.<sup>3,17</sup>
  - ▶ Also see NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal, Endometrial, and Gastric<sup>c</sup> and NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian, Pancreatic, and Prostate<sup>d</sup>.
- Environmental factors
  - ▶ Tanning bed use<sup>3,18,19</sup>
  - ▶ Residence in sunnier climate/latitude nearer to equator<sup>20</sup>
  - ▶ Intermittent, intense sun exposure (for truncal/extremity melanomas)<sup>3</sup>
  - ▶ Chronic sun exposure (for head/neck/arm melanomas)

<sup>a</sup> Risk factors for development of single or multiple primary melanomas, including subsequent primaries after index diagnosis. This list does not include risk factors for melanoma recurrence or progression, as those are covered elsewhere in the algorithm. Cutaneous melanoma is not a risk factor for uveal melanoma.

<sup>\*</sup> Available online, in these guidelines, at NCCN.org. <sup>†</sup> To view the most recent version of these guidelines, visit NCCN.org.

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**References<sup>\*</sup>**

**ME-A  
1 OF 2**

**Figure 1.** ME-A. NCCN Clinical Practice Guidelines in Oncology for Melanoma: Cutaneous, Version 2.2026.