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Melanoma: assessment and management summary of the 2022 update of the National Institute for Health and Care Excellence guidelines

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Abstract

Melanoma is the fifth most common cancer in the UK, accounting for 4% of all new cases of cancer, with a predicted 7% increase in incidence between 2014 and 2035. In parallel, since the initial publication of the National Institute for Health and Care Excellence (NICE) melanoma guidelines in 2015, there has been a paradigm shift in the management of the disease, with the introduction of effective systemic therapies. These innovations have reshaped the management of melanoma throughout the patient journey, and improved clinical outcomes. Surgical management has evolved, with the role of sentinel node biopsy in staging and management of regional lymph nodes becoming clearly defined, and a reduction in the need and indications for morbid block dissections. In advanced disease, effective therapies have allowed a de-escalation of surgery, changing the role and sequencing of local therapies. Regional therapies for in-transit disease have expanded and are effective in controlling this pattern of disease as part of multidisciplinary care. These advances have undoubtedly improved the care for people with melanoma, but they have also increased the complexity of management. In this context, this article seeks to summarize the most relevant of the recent updates to the NICE guidelines.

Lay summary

Melanoma is a common skin cancer in the UK. There are over 17,000 new cases diagnosed every year, which makes it the fifth most common cancer.

There have been recent developments in the treatment available for people with melanoma. One example is drugs that help the patient's immune system to fight melanoma cancer. At the same time, surgical techniques have evolved.

These new therapies mean that some patients will need less extensive operations. This is especially important in the lymph node area. These developments are improving care for people with melanoma. Yet, there are other complexities and considerations needed when deciding treatment.

As a result, it was necessary to revise the current clinical guidelines. In 2022 the National Institute for Health and Care Excellence (NICE) updated its recommendations. In the current study, a group of experts in the UK summarize the most recent updates in the NICE guidelines.

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What is already known about this topic?

- There has been a paradigm shift in melanoma management with the development of effective systemic therapies and de-escalation of surgical interventions.
- The evidence is challenging to synthesize into a set of guidelines, and there are areas that are already proving controversial.

What does this study add?

- New recommendations include the reduction of follow-up for stage IA melanoma, and increased surveillance for stage IIIA and higher melanoma.
- Other areas of change are less controversial, such as advising sentinel lymph node biopsy, and confirming the primacy of combination immunotherapy as the first treatment of stage IV melanoma, but they still represent a significant change in practice.

Context

The updated National Institute for Health and Care Excellence (NICE) guideline for melanoma covers assessment and management of melanoma in children, young people and adults. It aims to reduce the variation in practice and improve survival. It is aimed at healthcare professionals in primary, secondary and tertiary care, as well as commissioners and providers for people with melanoma and their families and carers.

The stages of melanoma in the guideline are based on the eighth edition of the Union for International Cancer Control (UICC) tumour–node–metastasis (TNM) classification of skin tumours and the American Joint Committee on Cancer (AJCC) melanoma staging system.

Recommendations

The recommendations presented are a summary of the 2022 update to the 2015 NICE guidelines. Where practice did not change, or where evidence for change was lacking, the guidance remains consistent with the 2015 guidelines. Each section of the guideline explains why the committee made the recommendations and how they might affect practice. In addition, full details of the evidence, including GRADE tables and the committee's discussion for each section, can be accessed via the published web resources for the NICE guidelines.[1,2]

The wording of the recommendations is in keeping with the NICE guidelines development manual, which advocates for clarity about what needs to be done, without the reader having to read the rationale or the committee's discussion in the evidence review document. This focuses on the action, with emphasis on the wording used depending on the strength of the recommendation.[3] NICE recommendations are constructed on the balance between the benefits and harms of an intervention, health economic considerations and the quality of the supporting evidence.

Some recommendations are made with more certainty than others, with recommendations expressed to reflect this. For example, where there is clear and strong evidence of benefit, the word 'offer' is used, and where the benefit is less certain 'consider' is used.[4] 'Offer', 'do not offer' and 'advise' are used for strong recommendations, while 'consider' is used for weaker ones.[5] Full details of the committee discussion, and the evidence used to arrive at recommendations, may be accessed in evidence reviews for each section. These include GRADE certainty, and are helpful to discern where recommendations were changed. This could be due to changes in evidence or practice, the strength of evidence, or the extent of literature assessment, or where there was not enough evidence to change a pre-existing recommendation.

Communication and support

Updates

Throughout their treatment, people with melanoma should be given information that is accurate and easy to understand. This should be tailored to their needs, and different media should be used. It is recommended that topics discussed should include:

- melanoma and different types of skin cancer
- treatment options with risks and benefits, and where your appointments will take place
- which healthcare professionals will undertake the care
- expected waiting times
- follow-up treatment.

Discussion should take place regarding recognizing signs and symptoms of suspicious skin lesions, how to prevent recurrence and sun damage, and how to avoid vitamin D deficiency. What to do if they have concerns about recurrence and how to access local services should also be discussed.[6,7]

Managing vitamin D levels and concurrent drug treatment

Updates

For patients diagnosed with melanoma, advice was given not to withhold or change drug treatment except for immunosuppressants and immunomodulators. For patients on immunosuppressive or immunomodulatory treatments, seek advice from the person's specialist team with the

Table 1 Recommendations for assessing melanoma

	Assessing melanoma	NICE recommendation
1	Do not offer BRAF analysis for stage IA or IB melanoma except as part of a clinical trial	Do not offer
2	BRAF analysis should be considered in stage IIA or IIB primary melanoma	Consider
3	All patients with stage IIC–IV primary melanoma should have BRAF analysis carried out	Advise
4	Local skin multidisciplinary teams should arrange BRAF analysis and state the preferred block	Offer
5	When performing BRAF analysis consider immunohistochemistry for BRAF V600E as the first test, if available	Consider
6	If immunohistochemistry is negative or inconclusive, a different genetic test should be used	Advise
7	BRAF analysis should be offered to patients if they are potential candidates for any ongoing clinical trials that require knowledge of genetic status	Advise

NICE, National Institute for Health and Care Excellence. The terms 'offer', 'do not offer' and 'advise' are used for strong recommendations, while 'consider' is used for weaker ones. An evidence GRADE summary is provided in Appendix S1 (see Supporting Information). Full evidence and economic analysis resources are available online.[9]

aim of optimizing quality of life while minimizing the person's risk.[8]

Assessing melanoma

Updates to the 2015 guidance

These updates are summarized in Table 1.[9]

BRAF analysis of primary melanoma tissue samples

Do not offer BRAF analysis for stage IA or IB melanoma except as part of a clinical trial. BRAF analysis should be considered in stage IIA or IIB primary melanoma. All patients with stage IIC–IV primary melanoma should have BRAF analysis carried out.

Local skin multidisciplinary teams (MDTs) should arrange BRAF analysis and state the preferred block. When performing BRAF analysis consider immunohistochemistry (IHC) for BRAF V600E as the first test, if available. If IHC is negative or inconclusive, a different genetic test should be used. BRAF analysis should be offered to patients if they are potential candidates for any ongoing clinical trials that require knowledge of the genetic status.

Discussion: rationale and impact of guidance

In the 2015 guidelines, genetic testing was recommended for melanoma of stage IIC and above, but not for stages IA or IB. The 2022 committee extended the guidance to include consideration of BRAF analysis for stage IIA or IIB and that it should be carried out for stage IIC–IV. Based on committee experience and the context of advances in targeted therapy, it was agreed that the extension of guidance would have practical utility. Disease relapse occurs in a significant proportion of people with stage IIA–IIC melanoma (up to 50% of people with stage IIC melanoma at 5 years). Therefore, knowing the BRAF status might speed up the decision making regarding treatment of relapse and optimize use of contemporary effective systemic therapies.

The committee advised that the analysis should be arranged by the local skin cancer MDT, to provide a more coordinated process, with the report of the primary lesion identifying the most appropriate block for analysis, as specified by the local dermatopathologist.

The 2015 guidelines did not specify what type of genetic test should be employed, whereas the 2022 committee evaluated specific types of tests. The committee concluded that IHC using BRAF V600E analysis is the most widely available, rapid test, which allows treatment to be started sooner than with other modalities. Evidence that IHC rarely produced false positives was noted. As false negatives do occur, it was agreed that a genetic test should be used to double-check a negative or inconclusive result. Genetic testing early in the melanoma pathway may also streamline enrolment into clinical trials and identify more candidates for trials.

The committee predicted that these recommendations might increase the use of genetic testing in general, and specifically increase the use of IHC to test for BRAF V600E. It was thought that this change might also reduce variations in genetic testing practice.

Staging with sentinel lymph node biopsy

Updates to the 2015 guidance

The recommendations for staging with sentinel lymph node biopsy (SLNB) are summarized in Table 2.[10]

Do not offer imaging or SLNB to people who have stage IA melanoma or evidence of microsatellites on their primary pathology. Do not offer imaging before SLNB unless lymph node or distant metastases are suspected. SLNB should be considered for people who have melanoma with a Breslow thickness of 0.8–1 mm and at least one of the following features: ulceration, lymphovascular invasion and a mitotic index of ≥ 2.

For people with melanoma with a Breslow thickness > 1.0 mm, SLNB should be considered. For women who are pregnant, the option of delaying the SLNB until after the pregnancy is completed should be discussed.

Consider staging with whole-body and brain contrast-enhanced computed tomography (CE-CT) for people with stage IIB melanoma. All patients with stage IIC–IV melanoma should be offered staging with whole-body and brain CE-CT. Staging with brain magnetic resonance imaging (MRI), instead of brain CE-CT, could be considered if locally available and if discussed with the skin MDT. Whole-body and brain MRI instead of CE-CT should be offered to children and young adults (birth to 24 years) with stage IIB–IV melanoma, and women with stage IIB–IV melanoma who are pregnant. A brain MRI should be considered instead of brain CE-CT for people with stage IIIC–IV melanoma and either a mitotic index ≥ 5 or a primary melanoma on the scalp.

Table 2 Recommendations for staging with sentinel lymph node biopsy (SLNB)

	Staging with SLNB	NICE recommendation
1	Do not offer imaging or SLNB to people who have stage IA melanoma or evidence of microsatellites on their primary pathology	Do not offer
2	Do not offer imaging before SLNB unless lymph node or distant metastases are suspected	Do not offer
3	SLNB should be considered for people who have melanoma with a Breslow thickness of 0.8–1 mm and at least one of the following features: ulceration, lymphovascular invasion, mitotic index ≥ 2	Consider
4	For people with melanoma with a Breslow thickness > 1.0 mm SLNB should be considered	Consider
5	Consider staging with whole-body and brain CE-CT for people with stage IIB melanoma	Consider
6	All patients with stage IIC–IV melanoma should be offered staging with whole-body and brain CE-CT	Offer
7	Staging with brain MRI, instead of brain CE-CT, could be considered if locally available and if discussed with the skin multidisciplinary team	Consider
8	Whole-body and brain MRI instead of CE-CT should be offered to children and young adults (birth to 24 years) with stage IIB–IV melanoma, and women with stage IIB–IV melanoma who are pregnant	Offer
9	A brain MRI should be considered instead of a brain CE-CT for people with stage IIIC–IV melanoma and either a mitotic index ≥ 5 or a primary melanoma on the scalp	Consider
10	Repeat staging imaging should be considered prior to starting adjuvant therapy unless imaging has been performed with results available within the last 8 weeks	Consider
11	Repeat staging imaging should be considered prior to starting adjuvant therapy unless imaging has been performed with results available within the last 8 weeks	Consider

CE-CT, contrast-enhanced computed tomography; MRI, magnetic resonance imaging; NICE, National Institute for Health and Care Excellence. The terms 'offer', 'do not offer' and 'advise' are used for strong recommendations, while 'consider' is used for weaker ones. An evidence GRADE summary is provided in Appendix S1 (see Supporting Information). Full evidence and economic analysis resources are available online.[10]

Repeat staging imaging should be considered prior to starting adjuvant therapy unless imaging has been performed and is available within the last 8 weeks.

Discussion: rationale and impact of guidance

Sentinel lymph node biopsy. Evidence showed that SLNB should be performed or ruled out before imaging for most people, because imaging does not accurately detect lymph node metastasis during staging. The committee agreed that imaging should only be offered before SLNB if lymph node or distant metastasis is suspected.

Specific factors predictive of positive SLNB were discussed, and the fact that this might not be a cost-effective intervention if the risk of metastasis is low. This has implications for patients whose melanomas have a Breslow thickness of 0.8–1 mm.

The committee discussed SLNB in pregnancy and agreed that in their experience no harm is associated with delaying SLNB until after pregnancy. However, that decision should be made within the specialist cancer MDT on a case-by-case basis after discussion with the person.

Imaging. There is less evidence on imaging during staging, with the committee agreeing that imaging should be consistent with the imaging during follow-up. However, evidence showed a high rate of recurrence in the interim period between surgery and starting adjuvant therapy. Therefore, the committee agreed that for people starting adjuvant therapy, staging imaging should have been performed within 8 weeks. This timeframe was based on the committee members' considered experience, noting that one study had defined this time interval at 7.4 weeks.

Current practice is commonly to offer SLNB to people with melanoma with a Breslow thickness of 0.8–1 mm. The recommendation is expected to reduce the volume of SLNBs in this group by targeting them to those with risk factors for a positive node. Ulceration is the most common risk factor for nodal positivity and is therefore likely to be the main reason for offering an SLNB. A mitotic rate ≥ 2 mm^{-2} in the primary tumour in this group is now also a factor for consideration of an SLNB.

Economic analysis recognized CT imaging as the most clinically accurate and cost-effective modality for staging patients with melanoma. It is expected that increased use of CT will reduce the current variability in imaging modalities currently employed in the UK.

Managing stage 0–II melanoma

Updates to the 2015 guidance

Table 3 summarizes the recommendations for stage 0–II melanoma.[11]

When excising a stage 0 melanoma, a clinical margin of ≥ 0.5 cm should be considered. If excision does not achieve an adequate histological margin, discuss further management with the specialist MDT.

When performing a further excision for melanoma, the clinical margin should be around the histological biopsy scar and take into account the primary melanoma margin. A clinical margin of 1-cm should be used when excising stage I melanoma, or when a 2-cm excision margin would cause unacceptable disfigurement or morbidity. A 2-cm margin should be used when excising stage II melanoma.

Discussion: rationale and impact of guidance

In 2015 the committee found no evidence on the optimal clinical margin for stage 0 melanoma. The 2022 committee found no further evidence and therefore the advice was retained. However, the committee acknowledged uncertainty about optimal excision margins and recommended research on the histological excision margins.

With regard to stage I and stage II melanoma, the 2015 committee's advice was retained, which is for 1-cm and

Table 3 Recommendations for managing stage 0–II melanoma

	Managing stage 0–II melanoma	NICE recommendation
1	When performing a further excision for melanoma, the clinical margin should be around the histological biopsy scar and take into account the primary melanoma margin	Advise
2	A clinical margin of 1-cm should be used when excising stage I melanoma, or when a 2-cm excision margin would cause unacceptable disfigurement or morbidity	Advise
3	A 2-cm margin should be used when excising stage II melanoma	Advise
4	If excision does not achieve an adequate histological margin, discuss further management with the specialist multidisciplinary team	Advise

The terms 'offer', 'do not offer' and 'advise' are used for strong recommendations. An evidence GRADE summary is provided in Appendix S1 (see Supporting Information). Full evidence and economic analysis resources are available online.[11]

2-cm excision, respectively, taking into account the smaller margin discussed with the skin cancer MDT in cosmetically and functionally sensitive areas.

Managing stage III melanoma

Updates to the 2015 guidance

Completion lymph node dissection should not be routinely offered to people with stage III melanoma and micrometastatic nodal disease detected by SLNB, unless there are factors that might make recurrent or progressive nodal disease difficult to manage and after discussion with the person and the specialist MDT. Examples of factors that could be considered include head and neck melanoma, people for whom adjuvant therapies for stage III melanoma are contraindicated, or where regular follow-up and nodal surveillance are not possible.

Discussion: rationale and impact of guidance

Completion lymph node dissection. The 2015 recommendation was amended as current evidence suggests that lymph node dissection for patients with stage III melanoma does not improve the overall survival or melanoma-specific survival compared with surveillance, and that it is associated with an increased risk of lymphoedema.

However, the committee recognized there may be less nodal basin control in patients who had SLNB and surveillance compared with the dissection, and acknowledged that certain factors might make it difficult to manage recurrent nodal disease. Therefore, they agreed that completion lymph node dissection could be considered for people with these factors.

Sentinel lymph node biopsy. The committee could find no evidence for the benefit of SLNB for patients whose primary lesion had evidence of microsatellites. The presence of these lesions upstages a patient to stage III, thereby negating the prognostic benefit of SLNB. Most centres do not currently offer SLNB to patients with stage IIIC disease, and therefore the committee agreed not to make recommendations in this area.

How the recommendation might affect practice. Completion lymph node dissection is no longer standard practice, and the recommendation will not affect this.

Treating in-transit metastasis in stage III and IV melanoma

Updates to the 2015 guidance

The management of in-transit metastases, including surgery or treatment in a regional specialist centre, should be discussed with the specialist MDT. Surgery should be offered as the first option. If it is not feasible, or if the person has recurrent in-transit metastases, consider one of the following options based on their suitability for the individual person:

- systemic anticancer therapy
- talimogene laherparepvec (T-VEC) in line with the NICE's technology appraisal guidance
- isolated limb infusion or perfusion
- radiotherapy
- electrochemotherapy
- a topical agent, such as imiquimod.

Discussion: rationale and impact of guidance

Good-quality evidence of localized treatment is lacking. Several treatment modalities are possible, and therefore the committee thought the decision should be based on the patient's suitability for each treatment. The committee removed the option of CO_2 laser listed in the 2015 guideline because it is no longer standard of care. A research recommendation was also made on the effectiveness of localized treatment.

Managing stage IV and unresectable stage III melanoma

Updates to the 2015 guidance

Surgery or other ablative treatment to prevent or control symptoms of oligometastatic stage IV melanoma should be considered in consultation with other site-specific MDTs (Table 4).[12]

For guidance on diagnosing, monitoring and managing brain metastasis in people aged > 16 years, reference should be made to the NICE guidelines on brain tumour (primary) and brain metastases in those aged > 16 years. People with melanoma and brain metastases who might be suitable for surgery or stereotactic radiotherapy should be referred to the neuro-oncology MDT for a recommendation about treatment.

When choosing systemic anticancer treatment for untreated stage IV or unresectable stage III melanoma, the

Table 4 Recommendations for managing stage IV and unresectable stage III melanoma

	Managing stage IV and unresectable stage III melanoma	NICE recommendation
1	Surgery or other ablative treatment to prevent or control symptoms of oligometastatic stage IV melanoma should be considered in consultation with other site-specific multidisciplinary teams	Consider
2	People with melanoma and brain metastases that might be suitable for surgery or stereotactic radiotherapy should be referred to the neuro-oncology multidisciplinary team for a recommendation about treatment	Advise
3	Treatment with immunotherapy should be offered to people with untreated stage IV or unresectable stage III melanoma	Offer
4	Nivolumab plus ipilimumab should be offered to people with untreated stage IV or unresectable stage III melanoma	Offer
5	If dual-agent therapy is unsuitable or unacceptable (e.g. potential toxicity), monotherapy with either pembrolizumab or nivolumab should be offered	Offer
6	If immunotherapy is contraindicated or unsuitable, encorafenib plus binimetinib, or dabrafenib plus trametinib should be considered	Consider
7	Offer targeted therapies for BRAF V600E mutations if it is predicted that there is not enough time for an adequate immune response – for example because of high disease burden or rapid progression	Offer
8	If encorafenib plus binimetinib, or dabrafenib plus trametinib are both unsuitable or unacceptable to the person, offer monotherapy, dabrafenib or vemurafenib to people for whom binimetinib and trametinib are contraindicated	Offer
9	If targeted treatment is contraindicated, consider treatment with chemotherapy (dacarbazine) or best supportive care	Consider
10	In patients in whom immunotherapies and targeted therapies are contraindicated, unsuitable or unacceptable, consider treatment with chemotherapy (dacarbazine) or best supportive care	Consider
11	Further cytotoxic chemotherapy should not be routinely offered after treatment with dacarbazine except in the context of a clinical trial	Do not offer
12	People with incurable melanoma should be referred to specialist palliative care services for symptom management	Advise

NICE, National Institute for Health and Care Excellence. The terms 'offer', 'do not offer' and 'advise' are used for strong recommendations, while 'consider' is used for weaker ones. An evidence GRADE summary is provided in Appendix S1 (see Supporting Information). Full evidence and economic analysis resources are available online.[12]

treatment decisions should be based on comorbidities and performance status, the risk of treatment toxicity, whether the potential treatment will be tolerated, the presence of symptomatic brain metastases, and tumour biology (e.g. high disease burden, rapid progression, lactate dehydrogenase level). Treatment decisions should be made after a full assessment of the risks and benefits by the treating physician and discussion with the person, in line with the NICE guideline on shared decision making.[7]

Treatment with immunotherapy should be offered to people with untreated stage IV or unresectable stage III melanoma. Nivolumab plus ipilimumab should be offered to people with untreated stage IV or unresectable stage III disease. If dual-agent therapy is unsuitable or unacceptable (e.g. potential toxicity), monotherapy with either pembrolizumab or nivolumab should be offered.

If immunotherapy is contraindicated or unsuitable, encorafenib plus binimetinib, or dabrafenib plus trametinib should be considered. Offer targeted therapies for BRAF V600E mutations also, if it is predicted that there is not enough time for an adequate immune response – for example because of high disease burden or rapid progression.

If encorafenib plus binimetinib, or dabrafenib plus trametinib are both unsuitable or unacceptable to the person, offer monotherapy, dabrafenib or vemurafenib to people for whom binimetinib and trametinib are contraindicated. If targeted treatment is contraindicated, consider treatment with chemotherapy (dacarbazine) or best supportive care.

When considering systemic anticancer treatment for people with previously treated stage IV or unresectable stage III melanoma, consideration would be given to the factors previously mentioned regarding immunotherapies. Similarly, in patients in whom immunotherapies and targeted therapies are contraindicated, unsuitable or unacceptable, consider treatment with chemotherapy (dacarbazine) or best supportive care. Further cytotoxic chemotherapy with dacarbazine should not be routinely offered post-treatment except in the context of a clinical trial.

People with incurable melanoma should be referred to specialist palliative care services for symptom management.[13]

Why the committee made the recommendations

The committee looked at the evidence on immunotherapies and targeted therapies, and they also compared health economic models, noting the complexities, nuances and treatment pathways. The evidence showed that, overall, immunotherapies are more clinically affected than targeted therapies. Within the immunotherapies nivolumab plus ipilimumab was the most clinically effective and cost-effective.

However, the risk of toxicity increases when immunotherapies are used in combination, and are higher for single-agent immunotherapy than for targeted therapies. Therefore, monotherapy should be an option for patients – for example those with poor performance status or comorbidities that are less likely to tolerate toxicity. Both nivolumab and pembrolizumab appear to have similar clinical effectiveness and cost-effectiveness, hence either could be used in that context.

NICE technology appraisal guidance recommends ipilimumab for untreated advanced melanoma. However, this was not included in the recommendation as either nivolumab or pembrolizumab monotherapy is commonly used in this population.

If immunotherapy is unsuitable the committee agreed that targeted therapies based on BRAF status are an option. For example, patients with symptomatic brain metastasis usually need steroids, which exclude treatment with immunotherapy. For people with high disease burden or rapid progression there may not be enough time to generate the necessary immune response that is associated with immunotherapy.

As regards targeted therapies, evidence showed that encorafenib plus binimetinib or trametinib plus dabrafenib had similar clinical effectiveness, and health economic modelling did not demonstrate clear differences in cost-effectiveness between these two options. Therefore, the committee agreed that either could be used. If these options are unsuitable, monotherapy with dabrafenib or vemurafenib should be offered.

If targeted treatment for BRAF-mutated melanoma is unsuitable or if the melanoma has a wildtype mutation, the committee agreed that options are limited to chemotherapy with dacarbazine or best supportive care.

Regarding previously treated stage IV and unresectable stage III disease, the evidence for clinical and cost-effectiveness of treatment in this area is limited. Therefore, the committee preferred to list all available treatment options and key factors that should be taken into account when considering treatment for previously treated melanoma.

No specific evidence was found of the effectiveness of systemic cancer therapy in children and young people with melanoma; however, the committee agreed treatment should not differ between adults and children.

The committee noted that people with incurable melanoma with high symptom burden should be managed at an early stage and recommended referral to specialist palliative care services.

How the recommendations might affect practice

The expectation would be that a higher proportion of patients are offered nivolumab plus ipilimumab as systemic treatment for stage IV and unresectable stage III melanoma.

Follow-up after treatment for melanoma

Updates to the 2015 guidance

Table 5 provides a summary of recommendations for follow-up after treatment.[14]

Information and support for people who have had melanoma

People who have completed treatment for melanoma should be given contact details for a specialist skin cancer service that can provide advice about problems or concerns related to the melanoma. The person, the family and carers in the family should be offered psychosocial support at all follow-up appointments. Local follow-up policies should also reinforce advice about self-examination and health promotion for people with melanoma and their families, including sun awareness and avoiding vitamin D depletion.[15] This should include advice on stopping smoking for people who smoke.

Exceptions to routine follow-up

For people with stage 0 melanoma, it is reasonable to provide advice at a clinic visit during the first year after treatment has been finished. This should include self-examination and health promotion for people with melanoma and their families, including sun awareness and protection, and avoiding vitamin D depletion. Advice on smoking cessation may also be given.

Personalized follow-up should be offered to patients with unresectable stage III or IV melanoma. Personalized follow-up can also be considered for patients at increased risk of further primary melanomas. Whole-body and brain MRI instead of CE-CT should be offered to children and young adults (< 24 years) having imaging as part of follow-up and for women who are pregnant. MRI of the brain should be offered for follow-up to people with known resected brain metastasis. MRI of the brain for follow-up imaging as opposed to CT may be considered after discussion with a specialist MDT.

Planning routine follow-up

Full examination of skin and regional lymph nodes at each clinic appointment should be performed by clinical health

Table 5 Recommendations for follow-up after treatment

	Follow-up after treatment for melanoma	NICE recommendation
1	People who have completed treatment for melanoma should be given contact details for a specialist skin cancer service that can provide advice about problems or concerns related to the melanoma	Advise
2	The person, the family and carers in the family should be offered psychosocial support at all follow-up appointments	Offer
3	Local follow-up policies should also reinforce advice about self-examination and health promotion for people with melanoma and their families, including sun awareness and avoiding vitamin D depletion. This should include advice on stopping smoking for people who smoke	Advise
4	Personalized follow-up should be offered to patients with unresectable stage III or IV melanoma	Offer
5	Personalized follow-up can also be considered for patients at increased risk of further primary melanomas	Consider
6	Whole-body and brain MRI instead of CE-CT should be offered to children and young adults (< 24 years) having imaging as part of follow-up and for women who are pregnant	Offer
7	MRI of the brain should be offered for follow-up to people with known resected brain metastasis	Offer
8	Full examination of skin and regional lymph nodes at each clinic appointment should be performed by clinical health professionals with skills and expertise in skin cancer and lymph node examination	Advise
9	Do not routinely use PET-CT during follow-up of patients with melanoma	Advise
10	For people having both CT scans and ultrasounds alternate between the two types of scans	Advise
11	Follow-up should be offered for 1 year to people who have stage IA melanoma and for 5 years to people who have stage IB–IV melanoma	Offer

CE-CT, contrast-enhanced computed tomography; MRI, magnetic resonance imaging; NICE, National Institute for Health and Care Excellence; PET, positron emission tomography. The terms 'offer', 'do not offer' and 'advise' are used for strong recommendations, while 'consider' is used for weaker ones. An evidence GRADE summary is provided in Appendix S1 (see Supporting Information). Full evidence and economic analysis resources are available online.[14]

Table 6 Follow-up after stage I–IV melanoma

Stage of melanoma	Follow-up
IA	Year 1. Consider two clinic appointments, with discharge at the end of year 1. Do not routinely offer screening investigations (including imaging and blood tests) as part of follow-up
IB	Year 1. Offer two clinic appointments, and consider adding two ultrasound scans of the draining nodal basin if SLNB was considered but not done Years 2 and 3. Offer one clinic appointment each year, and consider adding one ultrasound scan of the draining nodal basin each year if SLNB was considered but not done Years 4 and 5. Offer one clinic appointment each year. Discharge at the end of year 5
IIA	Years 1 and 2. Offer two clinic appointments each year, and consider adding two ultrasound scans of the draining nodal basin each year if SLNB was considered but not done Year 3. Offer one clinic appointment, and consider adding one ultrasound scan of the draining nodal basin if SLNB was considered but not done Years 4 and 5. Offer one clinic appointment each year. Discharge at the end of year 5
IIB	Years 1 and 2. Offer four clinic appointments each year and consider two whole-body and brain CE-CT scans each year. Consider adding two ultrasound scans of the draining nodal basin each year if SLNB was considered but not done Year 3. Offer two clinic appointments and consider two whole-body and brain CE-CT scans. Consider adding two ultrasound scans of the draining nodal basin if SLNB was considered but not done Years 4 and 5. Offer one clinic appointment each year and consider one whole-body and brain CE-CT scan each year. Discharge at the end of year 5
IIC	Years 1 and 2. Offer four clinic appointments and two whole-body and brain CE-CT scans each year. Consider adding two ultrasound scans of the draining nodal basin each year if SLNB was considered but not done Year 3. Offer two clinic appointments and two whole-body and brain CE-CT scans. Consider adding two ultrasound scans of the draining nodal basin if SLNB was considered but not done Years 4 and 5. Offer one clinic appointment and one whole-body and brain CE-CT scan each year. Discharge at the end of year 5
IIIA to IIIC not currently having adjuvant therapy	Years 1–3. Offer four clinic appointments and two whole-body and brain CE-CT scans each year. Consider adding two ultrasound scans of the draining nodal basin each year if the person has a positive sentinel lymph node Years 4 and 5. Offer two clinic appointments and one whole-body and brain CE-CT scan each year. Discharge at the end of year 5
IIID and resected IV not currently having adjuvant therapy	Years 1–3. Offer four clinic appointments and four whole-body and brain CE-CT scans each year Years 4 and 5. Offer two clinic appointments and two whole-body and brain CE-CT scans each year. Discharge at the end of year 5
IIID and resected IV not currently having adjuvant therapy	During adjuvant therapy, base follow-up on therapeutic requirements

CE-CT, contrast-enhanced computed tomography; SLNB, sentinel lymph node biopsy. The terms 'offer', 'do not offer' and 'advise' are used for strong recommendations, while 'consider' is used for weaker ones. An evidence GRADE summary is provided in Appendix S1 (see Supporting Information). Full evidence and economic analysis resources are available online.[14]

professionals with skills and expertise in skin cancer and lymph node examination. They should have access to dermoscopy and medical photography as part of the examinations. For people having both CT scans and ultrasounds, alternate between the two types of scans. Do not routinely use positron emission tomography (PET) and CT during follow-up of patients with melanoma. Follow-up should be offered for 1 year to people who have stage IA melanoma and for 5 years to people who have stage IB–IV melanoma (Table 6).

Why the committee made the recommendations

Information and support for people with melanoma

The committee agreed that based on experience, the information given to patients with melanoma varies, and it is important to give patients support contact details if they have questions and concerns after treatment. Therefore, the committee agreed to retain the 2015 recommendation to provide psychosocial support and provision of advice on local follow-up policies. The committee noted a lack of evidence on the views of people who survive melanoma and made a recommendation for research on survivorship.

Exceptions to routine follow-up

Based on experience the committee agreed that people who have completed treatment for stage 0 melanoma can be discharged after a clinic visit for advice. They also identified groups who should be offered personalized follow-up, including patients with unresectable melanoma and those at increased risk of further melanomas. The committee also identified groups in whom MRI should be considered as a substitute for CE-CT.

Frequency of follow-up

The committee sought to find the optimal frequency of clinical follow-up. This should balance the need for prompt identification of recurrence or progression with the need to reduce the burden of follow-up for patients, and avoid the costs of unnecessary follow-up.

Evidence showed that people with treated stage IB–IIC disease who had a lower frequency of follow-up visits did not experience an increase in mortality, more cancer

recurrence or worsening quality of life. Therefore, the committee agreed to reduce the frequency of follow-up visits. Recommendations for clinic visits after resected stage III–IV disease were made to allow for a clinic visit after each imaging scan.

Imaging during follow-up

The committee agreed that CT scanning during follow-up should include the head because of the high frequency of brain metastasis, and because the risk of radiation exposure is not serious, but that brain MRI could be considered instead. There would be obvious logistical difficulties and increased resource implications for MRI use, and this should be discussed in the skin MDT, as there is a potential to reduce radiation exposure and potentially increase the accuracy of assessing brain metastasis.

Evidence regarding stage III melanoma suggested that PET-CT may be more sensitive for detecting metastasis; however, compared with CE-CT it was not cost-effective. Frequent imaging with CE-CT in the first 2–3 years would ensure timely identification of recurrence. Due to the high risk of recurrence with stage IIC melanoma, which is of higher frequency than stage IIIA melanoma, imaging should be offered at the same frequency as for stage III disease. The committee decided that CT imaging should be considered after stage IIB melanoma is confirmed.

The committee agreed that MRI should be offered for children and young adults having imaging as part of their surveillance, as opposed to CT scanning.

Ultrasound scanning was demonstrated by the evidence to be more sensitive than clinical examination as an alternative to CT and for detecting local lymph node metastasis. Using CT alone can miss or delay detection of lymph node recurrences. However, after extensive discussion, it was decided there was not sufficient-quality evidence to show that ultrasound reduces mortality or time to recurrence in people with a positive sentinel node. Moreover, and currently good practice, patients with a positive sentinel node are offered frequent cross-sectional imaging and it is unclear whether ultrasound offers practical benefits above and beyond this.

The guideline does not recommend completion lymph node dissection based on evidence comparing it with ultrasound scanning. However, there is no evidence comparing completion dissection with surveillance alone without ultrasound scanning. In addition, evidence suggests that most nodal recurrences develop within the first few years of diagnosis. The committee noted that the nodal status is unknown in patients who have not had SLNB, and thus the staging is incomplete. Based on this, the committee agreed to recommend ultrasound surveillance for 3 years for people with a positive sentinel lymph node and those were considered for, but did not have, SLNB.

The committee acknowledged the practical implications of ultrasound imaging during follow-up, such as the capacity to provide increased numbers of scans and the variable experience of healthcare professionals involved in follow-up. They recognized the need for more evidence to inform future guidance and made recommendations for research on surveillance strategies.

How the recommendations might affect practice

Current practice varies and these recommendations may help standardize practice across centres. Clinic visits for people with melanoma of stages I–IIC may be reduced, especially for people with stage I melanoma. The use of ultrasound CT or MRI scanning is expected to increase but the use of PET-CT is expected to decrease.

Recommendations for research

The guidelines committee also made the following recommendations for research. These are newly recommended areas of research, derived from the evidence gaps identified during the guideline generation process.

1. **Monitoring and response biomarkers**
   Can biomarkers accurately classify recurrence, progression and response to treatment?
2. **Safety, prognostic and predictive biomarkers**
   Can biomarkers be used for risk stratification and treatment planning for people with melanoma?
3. **Effectiveness of localized treatment**
   What is the effectiveness of localized treatment for patients with stage III and IV melanoma?
4. **Histological margins**
   What is the optimal histological excision margin in stage 0 melanoma?
5. **Surveillance strategies**
   How frequently should surveillance imaging be conducted, and which imaging modality should be used for people with stage IIB–IIIC melanoma?

Other recommendations included examining the experiences of people who are living with, through and beyond the melanoma diagnosis, in terms of survivorship on their disease journey.

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Conflicts of interest

M.J.S. has received consultancy fees from Amgen and Deciphera, as well as travel expenses from Stryker and Deciphera. He is the chair of the Melanoma Focus Anorectal Urogenital Melanoma guidelines committee. L.A.J. has a private practice for Spire Histopathology Services and a private practice for Dermis LLP. She is also the chief examiner for the Diploma in Dermatopathology for the Royal College of Pathology. The NICE policy on declaring and managing interests was followed throughout the guideline development

process (https://www.nice.org.uk/Media/Default/About/Who-we-are/Policies-and-procedures/declaration-of-interests-policy.pdf).

Data availability

The full current NICE melanoma guidelines, with the available tools, resources and evidence, can be found through their online portal at www.nice.org.uk/guidance/ng14.

Ethics statement

Not applicable.

Patient consent

Not applicable.

Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website.

References

1 National Institute for Health and Care Excellence. Melanoma: assessment and management. Tools and resources. Available at: https://www.nice.org.uk/guidance/ng14/resources (last accessed 30 January 2025).
2 National Institute for Health and Care Excellence. Melanoma: assessment and management. Evidence. Available at: https://www.nice.org.uk/guidance/ng14/evidence (last accessed 30 January 2025).
3 National Institute for Health and Care Excellence. Developing NICE guidelines: the manual. Available at: https://www.nice.org.uk/process/pmg20/chapter/interpreting-the-evidence-and-writing-the-guideline#wording-the-recommendations (last accessed 30 January 2025).
4 National Institute for Health and Care Excellence. Making decisions using NICE guidelines. Available at: https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-guidelines/making-decisions-using-nice-guidelines (last accessed 30 January 2025).
5 National Institute for Health and Care Excellence. Developing NICE guidelines: the manual. Strength of recommendations. Available at: www.nice.org.uk/process/pmg20/chapter/interpreting-the-evidence-and-writing-the-guideline#strength-of-recommendations (last accessed 30 January 2025).
6 National Institute for Health and Care Excellence. Patient experience in adult NHS services: improving the experience of care for people using adult NHS services. Available at: https://www.nice.org.uk/guidance/cg138 (last accessed 30 January 2025).
7 National Institute for Health and Care Excellence. Shared decision making. Available at: https://www.nice.org.uk/guidance/ng197 (last accessed 30 January 2025).
8 National Institute for Health and Care Excellence. Melanoma: assessment and management. NICE guideline NG14. Available at: https://www.nice.org.uk/guidance/ng14 (last accessed 30 January 2025).
9 National Institute for Health and Care Excellence. Melanoma: assessment and management. [A] Evidence reviews for genetic testing for melanoma. Available at: https://www.nice.org.uk/guidance/ng14/evidence/a-genetic-testing-for-melanoma-pdf-11141087294 (last accessed 30 January 2025).
10 National Institute for Health and Care Excellence. Melanoma: assessment and management. [B] Evidence review for the use of sentinel lymph node biopsy in people with melanoma. Available at: https://www.nice.org.uk/guidance/ng14/evidence/b-use-of-sentinel-lymph-node-biopsy-in-people-with-melanoma-pdf-11141087295 (last accessed 30 January 2025).
11 National Institute for Health and Care Excellence. Melanoma: assessment and management. [C] Evidence review for surgical and histological excision margins for people with stage 0 to II melanoma. Available at: https://www.nice.org.uk/guidance/ng14/evidence/c-surgical-and-histological-excision-margins-for-people-with-stage-0-to-ii-melanoma-pdf-11141087296 (last accessed 30 January 2025).
12 National Institute for Health and Care Excellence. Melanoma: assessment and management. [F] Evidence review for systemic and localised anticancer treatment for people with stage IV and unresectable stage III melanoma 2022. Available at: https://www.nice.org.uk/guidance/ng14/evidence/f-systemic-and-localised-anticancer-treatment-for-people-with-stage-iv-and-unresectable-stage-iii-melanoma-pdf-11141087299 (last accessed 30 January 2025).
13 National Institute for Health and Care Excellence. End of life care for adults: service delivery. NICE guideline NG142. Available at: https://www.nice.org.uk/guidance/ng142 (last accessed 30 January 2025).
14 National Institute for Health and Care Excellence. Melanoma: assessment and management. [G] Evidence review for the follow-up of people with melanoma. Available at: https://www.nice.org.uk/guidance/ng14/evidence/g-followup-of-people-with-melanoma-pdf-11141087300 (last accessed 30 January 2025).
15 National Institute for Health and Care Excellence. Sunlight exposure: risks and benefits. Available at: https://www.nice.org.uk/guidance/ng34/resources/sunlight-exposure-risks-and-benefits-pdf-1837392363205 (last accessed 30 January 2025).

Appendix 1 NICE Melanoma Assessment and Management guideline committee

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