NICE National Institute for Health and Care Excellence

NICE guideline

Melanoma: assessment and management

NICE guideline

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Introduction

Melanoma is the third most common skin cancer in the UK. It accounts for more cancer deaths than all other skin cancers combined. In 2011 there were 13,348 new cases of melanoma and 2209 deaths from melanoma.

Although melanoma is more often diagnosed in older people, it is increasingly affecting younger people. More than 900 adults aged under 35 are now diagnosed with melanoma annually in the UK, and it is the second most common cancer in adults aged between 25 and 49. Melanoma therefore leads to more years of life lost overall than many more common cancers.

Most melanomas occur in people with pale skin. The risk factors are skin that tends to burn in the sun, having many moles, intermittent sun exposure and sunburn.

This guideline addresses areas where there is uncertainty or variation in practice. It contains recommendations on:

- assessing and staging melanoma, including the use of sentinel lymph node biopsy
- treating stages 0–IV melanoma, including adjuvant chemotherapy and immunotherapy
- treating in-transit melanoma metastases
- treating metastatic melanoma
- follow-up after treatment for melanoma.

The guideline also includes advice on managing vitamin D levels and drug therapy for intercurrent conditions in people diagnosed with melanoma.

The guideline covers suspected or newly diagnosed cutaneous melanoma (including vulval and penile melanoma) in children, young people and adults. However, there was insufficient high-quality evidence on which to make specific recommendations for vulval and penile melanoma.

It does not cover primary ocular melanoma or melanoma arising in mucosal sites.

Safeguarding children

Remember that child maltreatment:

- is common
- can present anywhere
- may co-exist with other health problems, including melanoma.

See the NICE guideline on child maltreatment for clinical features that may be associated with maltreatment.

Medicines

The guideline will assume that prescribers will use a medicine's summary of product characteristics to inform decisions made with individual patients.

This guideline recommends some medicines for indications for which they do not have a UK marketing authorisation at the date of publication, if there is good evidence to support that use. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or those with authority to give consent on their behalf) should provide informed consent, which should be documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information. Where recommendations have been made for the use of medicines outside their licensed indications ('off-label use'), these medicines are marked with a footnote in the recommendations.

Patient-centred care

This guideline offers best practice advice on the care of children, young people and adults with suspected or diagnosed melanoma.

Patients and healthcare professionals have rights and responsibilities as set out in the NHS Constitution for England – all NICE guidance is written to reflect these. Treatment and care should take into account individual needs and preferences. Patients should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If the patient is under 16, their family or carers should also be given information and support to help the child or young person to make decisions about their treatment. Healthcare professionals should follow the Department of Health's advice on consent. If someone does not have capacity to make decisions, healthcare professionals should follow the code of practice that accompanies the Mental Capacity Act and the supplementary code of practice on deprivation of liberty safeguards.

NICE has produced guidance on the components of good patient experience in adult NHS services. All healthcare professionals should follow the recommendations in patient experience in adult NHS services.

If a young person is moving between paediatric and adult services, care should be planned and managed according to the best practice guidance described in the Department of Health's Transition: getting it right for young people.

Adult and paediatric healthcare teams should work jointly to provide assessment and services to young people with suspected or diagnosed melanoma. Diagnosis and management should be reviewed throughout the transition process, and there should be clarity about who is the lead clinician to ensure continuity of care.

Key priorities for implementation

The following recommendations have been identified as priorities for implementation. The full list of recommendations is in section 1.

See implementation: getting started for information about putting the recommendations on dermoscopy, managing suboptimal vitamin D levels, sentinel lymph node biopsy and completion lymphadenectomy into practice.

Communication and support

- To help people make decisions about their care, follow the recommendations on communication, information provision and support in NICE's guideline on improving outcomes for people with skin tumours including melanoma, in particular the following 5 recommendations:
    - 'Improved, preferably nationally standardised, written information should be made available to all patients. Information should be appropriate to the patients' needs at that point in their diagnosis and treatment, and should be repeated over time. The information given must be specific to the histopathological type of lesion, type of treatment, local services and any choice within them, and should cover both physical and psychosocial issues.'
    - 'Those who are directly involved in treating patients should receive specific training in communication and breaking bad news.'
    - 'Patients should be invited to bring a companion with them to consultations.'
    - 'Each LSMDT [local hospital skin cancer multidisciplinary team] and SSMDT [specialist skin cancer multidisciplinary team] should have at least one skin cancer clinical nurse specialist (CNS) who will play a leading role in supporting patients and carers. There should be equity of access to information and support regardless of where the care is delivered.'
    - 'All LSMDTs and SSMDTs should have access to psychological support services for skin cancer patients.'

Assessing melanoma

Dermoscopy and other visualisation techniques

- Assess all pigmented skin lesions that are either referred for assessment or identified during follow-up in secondary or tertiary care, using dermoscopy carried out by healthcare professionals trained in this technique.

Photography

- For a clinically atypical melanocytic lesion that does not need excision at first presentation in secondary or tertiary care:
  - use baseline photography (preferably dermoscopic) **and**
  - review the clinical appearance of the lesion, and compare it with the baseline photographic images, 3 months after first presentation to identify early signs of melanoma.

Taking tumour samples for genetic testing

- If targeted systemic therapy is a treatment option, offer genetic testing using:
  - a secondary melanoma tissue sample if there is adequate cellularity **or**
  - a primary melanoma tissue sample if a secondary sample is not available or is of inadequate cellularity.

Managing suboptimal vitamin D levels

- Measure vitamin D levels at diagnosis in secondary care in all people with melanoma.

Staging investigations

Sentinel lymph node biopsy

- Consider sentinel lymph node biopsy as a staging rather than a therapeutic procedure for people with stage IB–IIC melanoma with a Breslow thickness of more than 1 mm, and give them detailed verbal and written information about the possible advantages and disadvantages, using the table below.

Possible advantages of sentinel lymph node biopsy	Possible disadvantages of sentinel lymph node biopsy
The operation helps to find out whether the cancer has spread to the lymph nodes. It is better than ultrasound scans at finding very small cancers in the lymph nodes.	The purpose of the operation is not to cure the cancer. There is no good evidence that people who have the operation live longer than people who do not have it.
The operation can help predict what might happen in the future. For example, in people with a primary melanoma that is between 1 and 4 mm thick: • around 1 out of 10 die within 10 years if the sentinel lymph node biopsy is negative • around 3 out of 10 die within 10 years if the sentinel lymph node biopsy is positive.	The result needs to be interpreted with caution. Of every 100 people who have a negative sentinel lymph node biopsy, around 3 will subsequently develop a recurrence in the same group of lymph nodes.
People who have had the operation may be able to take part in clinical trials of new treatments for melanoma. These trials often cannot accept people who haven't had this operation.	A general anaesthetic is needed for the operation.
	The operation results in complications in between 4 and 10 out of every 100 people who have it.

Managing stage III melanoma

Completion lymphadenectomy

- Consider completion lymphadenectomy for people whose sentinel lymph node biopsy shows micro-metastases and give them detailed verbal and written information about the possible advantages and disadvantages, using the table below.

Possible advantages of completion lymphadenectomy	Possible disadvantages of completion lymphadenectomy

Removing the rest of the lymph nodes before cancer develops in them reduces the chance of the cancer returning in the same part of the body.	Lymphoedema (long-term swelling) may develop, and is most likely if the operation is in the groin and least likely in the head and neck.
The operation is less complicated and safer than waiting until cancer develops in the remaining lymph nodes and then removing them.	In 4 out of 5 people, cancer will not develop in the remaining lymph nodes, so there is a chance that the operation will have been done unnecessarily.
People who have had the operation may be able to take part in clinical trials of new treatments to prevent future melanoma. These trials often cannot accept people who have not had this operation.	There is no evidence that people who have this operation live longer than people who do not have it.
	Having any operation can cause complications.

Adjuvant radiotherapy

- Do not offer adjuvant radiotherapy to people with stage IIIB or IIIC melanoma unless a reduction in the risk of local recurrence is estimated to outweigh the risk of significant adverse effects.

Follow-up after treatment for melanoma

Follow-up for all people who have had melanoma

- Consider personalised follow-up for people who are at increased risk of further primary melanomas (for example people with atypical mole syndrome, previous melanoma, or a history of melanoma in first-degree relatives or other relevant familial cancer syndromes).

Follow-up after stage IIC melanoma with no sentinel lymph node biopsy or stage III melanoma

- Consider surveillance imaging as part of follow-up for people who have had stage IIC melanoma with no sentinel lymph node biopsy or stage III melanoma and who would become eligible for systemic therapy as a result of early detection of metastatic disease if:
    - there is a clinical trial of the value of regular imaging **or**

- the specialist skin cancer multidisciplinary team agrees to a local policy and specific funding for imaging 6-monthly for 3 years is identified.

Take into account the possible advantages and disadvantages of surveillance imaging and discuss these with the person, using the table below.

Possible advantages of surveillance imaging (having regular scans)	Possible disadvantages of surveillance imaging (having regular scans)
If the melanoma comes back (recurrent melanoma), it is more likely to be detected sooner. It is possible that this could lead to a better outcome by allowing treatment with drugs (such as immunotherapy drugs) to start earlier.	Although early drug treatment of recurrent melanoma might improve survival, there is currently no evidence showing this.
Some people find it reassuring to have regular scans.	Some people find that having regular scans increases their anxiety.
	Scans expose the body to radiation, which can increase the risk of cancer in the future.
	Scans of the brain and neck increase the risk of developing cataracts.
	Scans of the chest cause a very small increase in the risk of thyroid cancer.
	Scans may show abnormalities that are later found to be harmless, causing unnecessary investigations and anxiety.

Stages of melanoma

The stages of melanoma referred to in this guideline are from the American Joint Committee on Cancer's Melanoma of the skin staging (7th edition).

Staging of primary melanoma can be carried out in 2 steps. The initial staging is based on the histopathological features reported by the pathologist looking at the microscopic sections of the tumour. The melanoma is staged as 0–IIC, based on factors such as the thickness of the tumour and the presence or absence of ulceration. In many hospitals in the UK, this first step is followed by the option of a second, which is a sampling of the lymph nodes most likely to contain secondary melanoma cells (sentinel lymph node biopsy). If a sentinel lymph node biopsy is performed and microscopic disease is detected, the melanoma becomes stage III. If no microscopic disease is detected then the initial stage is used.

1 Recommendations

The following guidance is based on the best available evidence. The full guideline gives details of the methods and the evidence used to develop the guidance.

The wording used in the recommendations in this guideline (for example, words such as 'offer' and 'consider') denotes the certainty with which the recommendation is made (the strength of the recommendation). See about this guideline for details.

These recommendations cover suspected and diagnosed melanoma. All recommendations relate to children, young people and adults unless specified otherwise.

1.1 Communication and support

1.1.1 To help people make decisions about their care, follow the recommendations on communication, information provision and support in NICE's guideline on improving outcomes for people with skin tumours including melanoma, in particular the following 5 recommendations:

- 'Improved, preferably nationally standardised, written information should be made available to all patients. Information should be appropriate to the patients' needs at that point in their diagnosis and treatment, and should be repeated over time. The information given must be specific to the histopathological type of lesion, type of treatment, local services and any choice within them, and should cover both physical and psychosocial issues.'
- 'Those who are directly involved in treating patients should receive specific training in communication and breaking bad news.'
- 'Patients should be invited to bring a companion with them to consultations.'
- 'Each LSMDT [local hospital skin cancer multidisciplinary team] and SSMDT [specialist skin cancer multidisciplinary team] should have at least one skin cancer clinical nurse specialist (CNS) who will play a leading role in supporting patients and carers. There should be equity of access to information and support regardless of where the care is delivered.'
- 'All LSMDTs and SSMDTs should have access to psychological support services for skin cancer patients.'

1.1.2 Follow the recommendations on follow-up in NICE's guideline on improving outcomes for people with skin tumours including melanoma, in particular the following 2 recommendations:

- 'All patients should be given written instruction on how to obtain quick and easy access back to see a member of the LSMDT/SSMDT when necessary.'
- 'All patients should be given both oral and written information about the different types of skin cancer and instruction about self-surveillance.'

1.1.3 Give people with melanoma and their families or carers advice about protecting against skin damage caused by exposure to the sun while avoiding vitamin D depletion.

1.1.4 Carry out a holistic needs assessment to identify the psychosocial needs of people with melanoma and their needs for support and education about the likelihood of recurrence, metastatic spread, new primary lesions and the risk of melanoma in their family members.

1.1.5 Follow the recommendations on communication and patient-centred care in NICE's guideline on patient experience in adult NHS services.

1.2 Assessing melanoma

Dermoscopy and other visualisation techniques

See implementation: getting started for information about putting recommendation 1.2.1 into practice.

1.2.1 Assess all pigmented skin lesions that are either referred for assessment or identified during follow-up in secondary or tertiary care, using dermoscopy carried out by healthcare professionals trained in this technique.

1.2.2 Do not routinely use confocal microscopy or computer-assisted diagnostic tools to assess pigmented skin lesions.

Photography

1.2.3 For a clinically atypical melanocytic lesion that does not need excision at first presentation in secondary or tertiary care:

- use baseline photography (preferably dermoscopic) **and**
- review the clinical appearance of the lesion, and compare it with the baseline photographic images, 3 months after first presentation to identify early signs of melanoma.

Assessing and managing atypical spitzoid lesions

1.2.4 Discuss all suspected atypical spitzoid lesions at the specialist skin cancer multidisciplinary team meeting.

1.2.5 Make the diagnosis of a spitzoid lesion of uncertain malignant potential on the basis of the histology, clinical features and behaviour.

1.2.6 Manage a spitzoid lesion of uncertain malignant potential as melanoma.

Taking tumour samples for genetic testing

1.2.7 If targeted systemic therapy is a treatment option, offer genetic testing using:

- a secondary melanoma tissue sample if there is adequate cellularity **or**
- a primary melanoma tissue sample if a secondary sample is not available or is of inadequate cellularity.

Genetic testing in early-stage melanoma

1.2.8 Do not offer genetic testing of stage IA–IIB primary melanoma at presentation except as part of a clinical trial.

1.2.9 Consider genetic testing of stage IIC primary melanoma or the nodal deposits or in-transit metastases for people with stage III melanoma.

1.2.10 If insufficient tissue is available from nodal deposits or in-transit metastases, consider genetic testing of the primary tumour for people with stage III melanoma.

1.3 Managing suboptimal vitamin D levels

See implementation: getting started for information about putting recommendations 1.3.1 and 1.3.2 into practice.

1.3.1 Measure vitamin D levels at diagnosis in secondary care in all people with melanoma.

1.3.2 Give people whose vitamin D levels are thought to be suboptimal advice on vitamin D supplementation and monitoring in line with local policies and NICE's guideline on vitamin D.

1.4 Managing concurrent drug treatment

1.4.1 Do not withhold or change drug treatment for other conditions, except immunosuppressants, on the basis of a diagnosis of melanoma.

1.4.2 Consider minimising or avoiding immunosuppressants for people with melanoma.

1.5 Staging investigations

Sentinel lymph node biopsy

See implementation: getting started for information about putting recommendation 1.5.2 into practice.

1.5.1 Do not offer imaging or sentinel lymph node biopsy to people who have stage IA melanoma or those who have stage IB melanoma with a Breslow thickness of 1 mm or less.

1.5.2 Consider sentinel lymph node biopsy as a staging rather than a therapeutic procedure for people with stage IB–IIC melanoma with a Breslow thickness of

more than 1 mm, and give them detailed verbal and written information about the possible advantages and disadvantages, using the table below.

Possible advantages of sentinel lymph node biopsy	Possible disadvantages of sentinel lymph node biopsy
The operation helps to find out whether the cancer has spread to the lymph nodes. It is better than ultrasound scans at finding very small cancers in the lymph nodes.	The purpose of the operation is not to cure the cancer. There is no good evidence that people who have the operation live longer than people who do not have it.
The operation can help predict what might happen in the future. For example, in people with a primary melanoma that is between 1 and 4 mm thick: • around 1 out of 10 die within 10 years if the sentinel lymph node biopsy is negative • around 3 out of 10 die within 10 years if the sentinel lymph node biopsy is positive.	The result needs to be interpreted with caution. Of every 100 people who have a negative sentinel lymph node biopsy, around 3 will subsequently develop a recurrence in the same group of lymph nodes.
People who have had the operation may be able to take part in clinical trials of new treatments for melanoma. These trials often cannot accept people who haven't had this operation.	A general anaesthetic is needed for the operation.
	The operation results in complications in between 4 and 10 out of every 100 people who have it.

Imaging

1.5.3 Offer CT staging to people with stage IIC melanoma who have not had sentinel lymph node biopsy, and to people with stage III or suspected stage IV melanoma.

1.5.4 Include the brain as part of imaging for people with suspected stage IV melanoma.

1.5.5 Consider whole-body MRI for children and young people (from birth to 24 years) with stage III or suspected stage IV melanoma.

1.6 Managing stages 0–II melanoma

Excision

1.6.1 Consider a clinical margin of at least 0.5 cm when excising stage 0 melanoma.

1.6.2 If excision for stage 0 melanoma does not achieve an adequate histological margin, discuss further management with the multidisciplinary team.

1.6.3 Offer excision with a clinical margin of at least 1 cm to people with stage I melanoma.

1.6.4 Offer excision with a clinical margin of at least 2 cm to people with stage II melanoma.

Imiquimod for stage 0 melanoma

1.6.5 Consider topical imiquimod[1] to treat stage 0 melanoma in adults if surgery to remove the entire lesion with a 0.5 cm clinical margin would lead to unacceptable disfigurement or morbidity.

1.6.6 Consider a repeat skin biopsy for histopathological assessment after treatment with topical imiquimod for stage 0 melanoma, to check whether it has been effective.

1.7 Managing stage III melanoma

Completion lymphadenectomy

See implementation: getting started for information about putting recommendation 1.7.1 into practice.

1.7.1 Consider completion lymphadenectomy for people whose sentinel lymph node biopsy shows micro-metastases and give them detailed verbal and written information about the possible advantages and disadvantages, using the table below.

Possible advantages of completion lymphadenectomy	Possible disadvantages of completion lymphadenectomy
Removing the rest of the lymph nodes before cancer develops in them reduces the chance of the cancer returning in the same part of the body.	Lymphoedema (long-term swelling) may develop, and is most likely if the operation is in the groin and least likely in the head and neck.
The operation is less complicated and safer than waiting until cancer develops in the remaining lymph nodes and then removing them.	In 4 out of 5 people, cancer will not develop in the remaining lymph nodes, so there is a chance that the operation will have been done unnecessarily.
People who have had the operation may be able to take part in clinical trials of new treatments to prevent future melanoma. These trials often cannot accept people who have not had this operation.	There is no evidence that people who have this operation live longer than people who do not have it.
	Having any operation can cause complications.

Lymph node dissection

1.7.2 Offer therapeutic lymph node dissection to people with palpable stage IIIB–IIIC melanoma or nodal disease detected by imaging.

Adjuvant radiotherapy

1.7.3 Do not offer adjuvant radiotherapy to people with stage IIIA melanoma.

1.7.4 Do not offer adjuvant radiotherapy to people with stage IIIB or IIIC melanoma unless a reduction in the risk of local recurrence is estimated to outweigh the risk of significant adverse effects.

Palliative treatment for in-transit metastases

1.7.5 Refer the care of all people with newly diagnosed or progressive in-transit metastases to the specialist skin cancer multidisciplinary team (SSMDT).

1.7.6 If palliative treatment for in-transit metastases is needed, offer palliative surgery as a first option if surgery is feasible.

1.7.7 If palliative surgery is not feasible for people with in-transit metastases, consider the following options:

- systemic therapy (for more information see recommendations 1.8.5–1.8.9)
- isolated limb infusion
- isolated limb perfusion
- radiotherapy
- electrochemotherapy in line with NICE's interventional procedure guidance on electrochemotherapy for metastases in the skin from tumours of non-skin origin and melanoma
- CO_2 laser
- a topical agent such as imiquimod[2].

Palliative treatment for superficial skin metastases

1.7.8 Consider topical imiquimod[2] to palliate superficial melanoma skin metastases.

1.8 Managing stage IV melanoma

Management of oligometastatic stage IV melanoma

1.8.1 Refer the care of people who appear to have oligometastatic melanoma to the specialist skin cancer multidisciplinary team (SSMDT) for recommendations about staging and management.

1.8.2 Consider surgery or other ablative treatments (including stereotactic radiotherapy or radioembolisation) to prevent and control symptoms of

oligometastatic stage IVmelanomain consultation with site-specific MDTs (such as an MDT for the brain or for bones).

Brain metastases

1.8.3 Discuss the care of people with melanoma and brain metastases with the SSMDT.

1.8.4 Refer people with melanoma and brain metastases that might be suitable for surgery or stereotactic radiotherapy to the brain and other central nervous system tumours MDT for a recommendation about treatment.

Systemic anticancer treatment

Targeted treatments

1.8.5 For adults, see NICE's technology appraisal guidance on dabrafenibfor treating unresectable or metastatic BRAF V600 mutation-positive melanoma[3].

1.8.6 For adults, 'Vemurafenib is recommended as an option for treating BRAF V600 mutation-positive unresectable or metastatic melanoma only if the manufacturer provides vemurafenib with the discount agreed in the patient access scheme'[4]. [This recommendation is from NICE's technology appraisal guidance on vemurafenib for treating locally advanced or metastatic BRAF V600 mutation-positive malignant melanoma.]

Immunotherapy

1.8.7 For adults, see NICE's technology appraisal guidance on ipilimumab for previously treated advanced (unresectable or metastatic) melanoma and ipilimumab for previously untreated advanced (unresectable or metastatic) melanoma[5].

Cytotoxic chemotherapy

1.8.8 Consider dacarbazine for people with stage IV metastatic melanoma if immunotherapy or targeted therapy are not suitable[6].

1.8.9 Do not routinely offer further cytotoxic chemotherapy for stage IV metastatic melanoma to people previously treated with dacarbazine except in the context of a clinical trial.

1.9 Follow-up after treatment for melanoma

Follow-up for all people who have had melanoma

1.9.1 Perform a full examination of the skin and regional lymph nodes at all follow-up appointments.

1.9.2 Consider personalised follow-up for people who are at increased risk of further primary melanomas (for example people with atypical mole syndrome, previous melanoma, or a history of melanoma in first-degree relatives or other relevant familial cancer syndromes).

1.9.3 Consider including the brain for people having imaging as part of follow-up after treatment for melanoma.

1.9.4 Consider imaging the brain if metastatic disease outside the central nervous system is suspected.

1.9.5 Consider CT rather than MRI of the brain for adults having imaging as part of follow-up or if metastatic disease is suspected.

1.9.6 Consider MRI rather than CT of the brain for children and young people (from birth to 24 years) having imaging as part of follow-up or if metastatic disease is suspected.

1.9.7 Provide psychosocial support for the person with melanoma and their family or carers at all follow-up appointments.

1.9.8 All local follow-up policies should include reinforcing advice about self-examination (in line with recommendation 1.1.2), and health promotion for people with melanoma and their families, including sun awareness, avoiding vitamin D depletion (in line with recommendation 1.1.3), and NICE guidance on smoking cessation.

1.9.9 Continue to manage drug treatment for other conditions in line with recommendations 1.4.1 and 1.4.2 after treatment for melanoma.

Follow-up after stage 0 melanoma

1.9.10 Discharge people who have had stage 0 melanoma after completion of treatment and provide advice in line with recommendation 1.9.8.

Follow-up after stage IA melanoma

1.9.11 For people who have had stage IA melanoma, consider follow-up 2–4 times during the first year after completion of treatment and discharging them at the end of that year.

1.9.12 Do not routinely offer screening investigations (including imaging and blood tests) as part of follow-up to people who have had stage IA melanoma.

Follow-up after stages IB–IIB melanoma or stage IIC melanoma (fully staged using sentinel lymph node biopsy)

1.9.13 For people who have had stages IB–IIB melanoma or stage IIC melanoma with a negative sentinel lymph node biopsy, consider follow-up every 3 months for the first 3 years after completion of treatment, then every 6 months for the next 2 years, and discharging them at the end of 5 years.

1.9.14 Do not routinely offer screening investigations (including imaging and blood tests) as part of follow-up to people who have had stages IB–IIB melanoma or stage IIC melanoma with a negative sentinel lymph node biopsy.

Follow-up after stage IIC melanoma with no sentinel lymph node biopsy or stage III melanoma

1.9.15 For people who have had stage IIC melanoma with no sentinel lymph node biopsy, or stage III melanoma, consider follow-up every 3 months for the first 3 years after completion of treatment, then every 6 months for the next 2 years, and discharging them at the end of 5 years.

1.9.16 Consider surveillance imaging as part of follow-up for people who have had stage IIC melanoma with no sentinel lymph node biopsy or stage III melanoma

and who would become eligible for systemic therapy as a result of early detection of metastatic disease if:

- there is a clinical trial of the value of regular imaging **or**
- the specialist skin cancer multidisciplinary team agrees to a local policy and specific funding for imaging 6-monthly for 3 years is identified.

Take into account the possible advantages and disadvantages of surveillance imaging and discuss these with the person, using the table below.

Possible advantages of surveillance imaging (having regular scans)	**Possible disadvantages of surveillance imaging (having regular scans)**
If the melanoma comes back (recurrent melanoma), it is more likely to be detected sooner. It is possible that this could lead to a better outcome by allowing treatment with drugs (such as immunotherapy drugs) to start earlier.	Although early drug treatment of recurrent melanoma might improve survival, there is currently no evidence showing this.
Some people find it reassuring to have regular scans.	Some people find that having regular scans increases their anxiety.
	Scans expose the body to radiation, which can increase the risk of cancer in the future.
	Scans of the brain and neck increase the risk of developing cataracts.
	Scans of the chest cause a very small increase in the risk of thyroid cancer.
	Scans may show abnormalities that are later found to be harmless, causing unnecessary investigations and anxiety.

Follow-up after stage IV melanoma

1.9.17 Offer personalised follow-up to people who have had stage IV melanoma.

[1] At the time of publication (July 2015) topical imiquimod did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

[2] At the time of publication (July 2015) topical imiquimod did not have a UK marketing authorisation for this indication or for use in children and young people. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

[3] Dabrafenib has a marketing authorisation in the UK in monotherapy for the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600 mutation.

[4] Vemurafenib has a UK marketing authorisation for 'the treatment of adult patients with BRAF V600 mutation-positive unresectable or metastatic melanoma'.

[5] Ipilimumab has a UK marketing authorisation for 'the treatment of advanced (unresectable or metastatic) melanoma in adults'.

[6] Although this use is common in UK clinical practice, at the time of publication (July 2015), dacarbazine did not have a UK marketing authorisation for this indication or for use in children and young people. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

2 Research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future.

2.1 Techniques for confirming a diagnosis in people with suspected atypical spitzoid melanocytic lesions

In people with reported atypical spitzoid lesions, how effective are fluorescence in-situ hybridization (FISH), comparative genomic hybridization (CGH) and tests to detect driver mutations compared with histopathological examination alone in predicting disease-specific survival?

This should be investigated in a prospective diagnostic study. Secondary outcomes should include sensitivity, specificity, accuracy, positive predictive value, disease-specific survival and progression-free survival.

Why this is important

Atypical spitzoid lesions continue to be diagnostically challenging. There are no reliably reproducible histological, immunohistochemistry or molecular features that allow exact typing and prognostic assessment of these lesions. The current 'gold standard' is histological examination with expert review, but it is not always possible to distinguish spitzoid melanoma from benign spitzoid melanocytic lesions.

Current molecular technologies such as FISH and CGH provide some help, but the results are difficult to interpret and may not be conclusive. Understanding and mapping changes in molecular pathways could predict outcome and inform individual treatment planning.

2.2 Surgical excision for people with lentigo maligna

For people with lentigo maligna (stage 0 in sun-damaged skin, usually on the face) how effective is Mohs micrographic surgery, compared with excision with a 0.5 cm clinical margin, in preventing biopsy-proven local recurrence at 5 years?

This should be investigated in a randomised controlled trial. Secondary outcomes should include cosmetic and functional outcomes.

Why this is important

Mohs micrographic surgery is a microscopically controlled surgical technique designed to allow complete excision of the tumour with minimal tissue loss. The technique can be useful for people with lentigo maligna because their lesions can be very large and located in a cosmetically sensitive site where surgery may cause significant scarring. However, the histological detection of small numbers of melanocytes at the edge of a sample is difficult, and can lead to false negative results. In addition, lentigo maligna may occur in an area of field change with a risk of skip lesions at the edge. Therefore, although Mohs micrographic surgery may ensure complete excision of lentigo maligna, it can be accompanied by the recurrence of a similar lesion in adjacent skin.

2.3 Follow-up surveillance imaging

In people treated for high-risk stage II and III melanoma, does regular surveillance imaging improve melanoma-specific survival compared with routine clinical follow-up alone?

This should be investigated in a randomised controlled trial. Secondary outcomes should include time to recurrence, site of recurrence, proportion of people receiving active therapy at recurrence, cost effectiveness and quality of life.

Why this is important

Until recently there have been no effective therapies for metastatic melanoma and no strong rationale for early detection of relapse through surveillance imaging. However, new, effective targeted treatments and immunotherapy agents are now available and further treatments are likely to become available in the near future. In particular, immunotherapy can offer long-term disease-free survival but takes a number of months to take effect. In this situation, early detection of relapse may identify people likely to be fit enough to receive the treatment for long enough to benefit.

Although early detection of relapse through surveillance imaging might appear likely to improve outcomes, there is no evidence to confirm this. In addition, routine imaging has resource implications and involves more hospital visits and increased radiation exposure for the person.

2.4 Vitamin D supplementation

In people with stage I–III melanoma does vitamin D supplementation improve overall survival?

This should be investigated in a placebo-controlled randomised trial. Secondary outcomes should include disease-specific survival and toxicity, including the development of renal stones and hypercalcaemia.

Why this is important

It has been reported that suboptimal levels of vitamin D at diagnosis are common in people with melanoma from the north of England and that higher levels are associated with lower melanoma-related mortality. However, vitamin D levels are higher in leaner, fitter people and the nature of the relationship between vitamin D levels and melanoma survival is unclear.

There are 2 adjuvant trials of vitamin D supplementation listed as active currently, 1 in Italy and 1 in Australia. However, there are many uncertainties about the design of vitamin D trials, which might become clearer in the next few years. These include the dose of vitamin D, use of concurrent aspirin therapy and the baseline level at which vitamin D supplementation would be started.

2.5 The effect of drug therapy for concurrent conditions on melanoma survival

In people diagnosed with melanoma what is the effect of drug therapy to treat concurrent conditions on disease-specific survival?

This should be investigated in a national prospective cohort study. Secondary outcomes should include overall survival and quality of life.

Why this is important

Drugs such as immunosuppressants and those used to treat conditions such as diabetes have effects that may affect survival in people with melanoma. For example metformin, the most frequently prescribed drug for type 2 diabetes, is thought to reduce overall cancer rates in people with diabetes but to increase mortality from melanoma in the approximately 40% of these people who have a somatic BRAF mutation.

There is a need to balance the risk of melanoma deaths with the benefits from the most effective treatment of the concurrent conditions. But there is currently no evidence to inform this decision.

3 Other information

3.1 Scope and how this guideline was developed

NICE guidelines are developed in accordance with a scope that defines what the guideline will and will not cover.

How this guideline was developed

NICE commissioned the National Collaborating Centre for Cancer to develop this guideline. The Centre established a Guideline Development Group (see section 4), which reviewed the evidence and developed the recommendations.

The methods and processes for developing NICE clinical guidelines are described in the guidelines manual.

3.2 Related NICE guidance

Further information is available on the NICE website.

Published

General

- Vitamin D (2014) NICE guideline PH56
- Neutropenic sepsis (2012) NICE guideline CG151
- Opioids in palliative care (2012) NICE guideline CG140
- Patient experience in adult NHS services (2012) NICE guideline CG138
- MIST therapy system for the promotion of wound healing in chronic and acute wounds (2011) NICE medical technology guidance 5
- Medicines adherence (2009) NICE guideline CG76
- Surgical site infection (2008) NICE guideline CG74
- Smoking cessation (2008) NICE guideline PH10

Condition-specific

- Suspected cancer: recognition and referral (2015) NICE guideline NG12
- Dabrafenib for treating unresectable or metastatic BRAF V600 mutation-positive melanoma (2014) NICE technology appraisal guidance 321
- Ipilimumab for previously untreated advanced (unresectable or metastatic) melanoma (2014) NICE technology appraisal guidance 319
- Electrochemotherapy for metastases in the skin from tumours of non-skin origin and melanoma (2013) NICE interventional procedure guidance 446
- Vemurafenib for treating locally advanced or metastatic BRAF V600 mutation-positive malignant melanoma (2012) NICE technology appraisal guidance 269
- Ipilimumab for previously treated advanced (unresectable or metastatic) melanoma (2012) NICE technology appraisal guidance 268
- Endoscopic radical inguinal lymphadenectomy (2011) NICE interventional procedure guidance 398
- Skin cancer prevention (2011) NICE guideline PH32
- Improving outcomes for people with skin tumours including melanoma (2010) NICE guideline CSGSTIM
- Improving outcomes in children and young people with cancer (2005) NICE guideline CSGCYP
- Improving supportive and palliative care for adults with cancer (2004) NICE guideline CSGSP

Under development

NICE is developing the following guidance:

- Sunlight exposure: communicating the benefits and risks to the general public. NICE guideline. Publication expected September 2015.
- Skin cancer: the VivaScope 1500 and 3000 systems for detecting and monitoring skin lesions. NICE diagnostics guidance. Publication expected November 2015.
- Pembrolizumab for treating unresectable, metastatic melanoma after progression with ipilimumab. NICE technology appraisal guidance. Publication expected December 2015.

- Dabrafenib and trametinib for treating advanced unresectable or metastatic BRAFV600 mutation-positive melanoma. NICE technology appraisal guidance. Publication expected August 2016.
- Ipilimumab for the adjuvant treatment of completely resected high risk stage III or IV melanoma. NICE technology appraisal guidance. Publication date to be confirmed.

4 The Guideline Development Group, National Collaborating Centre and NICE project team, and declarations of interests

4.1 Guideline Development Group

Gill Godsell
Nurse Consultant (Skin Cancer), Nottingham NHS Treatment Centre

LaszloIgali
Consultant Histopathologist, Norfolk and Norwich University Hospital NHS Foundation Trust

Richard Jackson
Patient and carer member

Charles Kelly
Consultant Clinical Oncologist, Northern Centre for Cancer Care, Freeman Hospital, Newcastle

Stephen Keohane
Consultant Dermatologist, Portsmouth Hospitals NHS Trust, Portsmouth Dermatology Centre

Fergus Macbeth (Chair)
Clinical adviser, Wales Cancer Trials Unit, Cardiff University

Julia Newton-Bishop (Clinical Lead)
Professor of Dermatology, University of Leeds

Christine Parkinson
Consultant in Medical Oncology, Addenbrooke's Hospital, Cambridge

Barry Powell
Consultant Plastic Surgeon, St George's Hospital, London

Saskia Reeken
Clinical Nurse Specialist, Skin Cancer and Dermatology, Kingston Hospital NHS Foundation Trust, Surrey

Rachael Robinson
GP, Stockwell Road Surgery, Knarlesborough, GPwSI Dermatology, Harrogate District Foundation Trust, GPwSI Durnford Dermatology, Middleton, Manchester

Simon Rodwell (from April 2013 until October 2013)
Patient and carer member

John Rouse (from November 2013)
Patient and carer member

Julia Schofield
Principal Lecturer, University of Herefordshire, Consultant Dermatologist, United Lincolnshire Hospitals NHS Trust

Jonathan Smith
Consultant Radiologist, Leeds Teaching Hospital Trust

Sara Stoneham
Paediatric and Adolescent Oncology Consultant, University College Hospital, London

Martin Telfer
Consultant Maxillofacial Surgeon, York Teaching Hospital NHS Foundation Trust

4.2 National Collaborating Centre for Cancer

Stephanie Arnold
Information Specialist

Nathan Bromham
Senior Researcher

Laura Bunting
Researcher

Andrew Champion
Centre Manager

John Graham
Director

Lianne Gwillim
Project Manager

James Hawkins
Health Economist

Coral McCarthy
Project Manager (from May 2014 until February 2015)

Angharad Morgan
Researcher

Delyth Morris
Information Specialist (until April 2014)

Susan O'Connell
Researcher

Matthew Prettyjohns
Senior Health Economist

4.3 NICE project team

Christine Carson
Guideline Lead

Mark Baker
Clinical Adviser

Katie Perryman Ford
Guideline Commissioning Manager

Jennifer Watson-Henry
Guideline Coordinator (until November 2014)

Thomas Feist
Guideline Coordinator (from November 2014)

Nichole Taske
Technical Lead

Bhash Naidoo
Health Economist

Judy McBride
Editor

4.4 Declarations of interests

The following members of the Guideline Development Group made declarations of interests. All other members of the Group stated that they had no interests to declare. The conflicts of interest policy (2007) was followed until September 2014, when an updated policy was published.

Member	Interest declared	Type of interest	Decision taken
Barry Powell	Received a fee from Roche for chairing an advisory board on BRAF inhibitors in malignant melanoma. Donate fee to charity.	Personal pecuniary; specific	Declare and withdraw from discussions on all topics regarding BRAF inhibitors until July 2013
Barry Powell	Novartis have offered a fee to take part in a future advisory board on MEK inhibitors in melanoma. Not yet accepted.	Personal pecuniary; specific	If accepted, declare and withdraw from discussions on all topics regarding the MEK inhibitors until 12 months after date of advisory board

Barry Powell	Enrols patients into the EORTC 18091 trial. No fee received for doing this and no involvement past enrolling of patients.	Personal non-pecuniary; specific	Declare and participate
Barry Powell	Principal investigator for the UK for the EORTC MINITUB study. Study not yet started. Funded by individual trusts.	Personal non-pecuniary; specific	Declare and participate
Barry Powell	Chair of the Pathway Group for Skin Cancer for the London Cancer Alliance (working group on provision of skin cancer care in London).	Personal non-pecuniary	Declare and participate
Barry Powell	Wrote an editorial for Surgery journal giving opinions on the management of malignant melanoma.	Personal non-pecuniary	Declare and participate
Barry Powell	Received reimbursement of travelling expenses and subsistence from IGEA for attending a meeting regarding data collection for electrochemotherapy.	Personal pecuniary; specific	Declare and participate
Christine Parkinson	Received a fee from Boehringer Ingelheim for attending an advisory board and giving advice on a trial for their ovarian cancer drug BIBF1120. Fee was donated to charity.	Personal pecuniary non-specific	Declare and participate
Christine Parkinson	Received reimbursement of registration fee and accommodation from Boehringer Ingelheim for attending the International Gynaecological Cancer Society conference.	Personal pecuniary interest, non-specific	Declare and participate
Christine Parkinson	Co-investigator on the COMBI-V study. Funded by GSK.	Non-personal pecuniary; specific	Declare and participate
Christine Parkinson	Co-investigator on PACMEL. Sponsored by University of Oxford. Funded by GSK.	Non-personal pecuniary; specific	Declare and participate

Christine Parkinson	Co-investigator on the Phase 1, Open Label, Dose Finding Study to Assess the Safety and Tolerability of IMCgp100, a Monoclonal T Cell Receptor Anti-CD3 scFv Fusion Protein in Patients With Advanced Malignant Melanoma. Sponsored and funded by Immunocore Ltd.	Non-personal pecuniary; specific	Declare and participate
Christine Parkinson	Co-investigator on NICAM. Sponsored by Royal Marsden Foundation Trust and Institute of Cancer Research. Funded by CTAAC.	Non-personal pecuniary; specific	Declare and participate
Christine Parkinson	Co-investigator on the IMAGE study. Funded by Bristol Myers Squibb.	Non-personal pecuniary; specific	Declare and participate
Christine Parkinson	Co-investigator on the SUAVE study. Sponsor is Clatterbridge Centre for Oncology NHS Trust. Funded by Pfizer Limited and CTAAC.	Non-personal pecuniary; specific	Declare and participate
Christine Parkinson	Co-investigator on the MelResist study. Funded by Cambridge University Hospitals NHS Foundation Trust.	Non-personal pecuniary; specific	Declare and participate
Christine Parkinson	Principle investigator on the PARAGON trial. Sponsored by NHS Greater Glasgow & Clyde. Funded by CRUK.	Non-personal pecuniary; non-specific	Declare and participate
Christine Parkinson	Received reimbursement of travel and subsistence expenses from CLOVIS for attending an investigator meeting for the ARIEL2 and ARIEL3 trials for ovarian cancer.	Personal pecuniary; non-specific	Declare and participate
Fergus Macbeth	Chief investigator of a CRUK-funded trial supported by Pfizer with free drug and unrestricted educational grant.	Non-personal pecuniary; non-specific	Declare and participate

Fergus Macbeth	Received reimbursement of travel and subsistence expenses for attending the World Lung Cancer conference.	Personal pecuniary, non-specific	Declare and participate
Gill Godsell	Received reimbursement of travel and subsistence expenses from Almirall (manufacturers of topical treatments for pre-cancerous lesions) for attending a European Academy of Dermatology and Venerology meeting.	Personal pecuniary; specific	Declare and participate
Gill Godsell	Vice Chair of the Karen Clifford Skin Cancer Charity, until November 2013. Gave advice on clinical aspects of skin cancer – not specific treatments.	Personal non-pecuniary	Declare and participate
Jonathan Smith	Reviewed a systematic review on PET-CT in stage III melanoma for publication in the Journal of Surgical Oncology.	Personal non-pecuniary; specific	Declare and participate
Jonathan Smith	Received reimbursement of subsistence and course fee from Nucletron for attending the annual UK prostate brachytherapy course.	Personal pecuniary; non-specific	Declare and participate
Jonathan Smith	Received travel and accommodation from the Royal College of Radiologists to give a lecture on 'how to run a radiology discrepancy' at the Royal College of Radiology autumn scientific meeting.	Personal pecuniary; non-specific	Declare and participate
Jonathan Smith	Reports CT studies in the STAR trial, which is an RCT multi-centre trial in drug therapy for metastatic renal cell cancer.	Non-specific	Declare and participate
Julia Newton-Bishop	Received an honorarium from Roche for giving advice on cutaneous toxicity from vemurafenib.	Personal pecuniary; specific	Declare and participate
Julia Newton-Bishop	Department research fund received payment from Roche for giving advice on cutaneous toxicity from vemurafenib.	Non-personal pecuniary	Declare and participate

Julia Newton-Bishop	Received reimbursement of travelling expenses from Irish Association of Dermatologists for giving a talk on vitamin D and melanoma.	Personal pecuniary; specific	Declare and participate
Julia Newton-Bishop	Received an honorarium from Irish Association of Dermatologists for giving a talk on vitamin D and melanoma.	Personal pecuniary; specific	Declare and participate
Julia Newton-Bishop	Received reimbursement of travelling expenses from the Melanoma Study Group for giving a talk at the Focus on Melanoma conference on the levels of vitamin D in melanoma patients.	Personal pecuniary; specific	Declare and participate
Julia Newton-Bishop	Received reimbursement of travelling expenses from Beatson Institute for attending a seminar and giving a talk on the genetics of susceptibility and survival of melanoma.	Personal pecuniary	Declare and participate
Julia Newton-Bishop	Received reimbursement of travelling expenses from London Strategic Health Authority for attending an ECRIC Cancer Registry meeting to discuss NCIN work designed to understand cancer registration.	Personal pecuniary; non-specific	Declare and participate
Julia Newton-Bishop	Received reimbursement of travelling expenses from Public Health England for chairing an NCIN Chair's meeting regarding national data collection on skin cancer.	Personal pecuniary; non-specific	Declare and participate
Julia Newton-Bishop	Received reimbursement of travelling expenses from Public Health England for chairing the skin SSCRG group covering national data collection on skin cancer.	Personal pecuniary; non-specific	Declare and participate

Julia Newton-Bishop	Received reimbursement of travelling expenses from conference organisers giving a talk on the genetics of melanoma survival at the 8th World Congress of Melanoma.	Personal pecuniary; specific	Declare and participate
Julia Newton-Bishop	Received reimbursement of travelling expenses from Public Health England for chairing an NCIN workshop on national data collection on skin cancer.	Personal pecuniary; non-specific	Declare and participate
Julia Newton-Bishop	Received reimbursement of travelling expenses from Roche for attending a meeting and giving a talk on the biology of melanoma.	Personal pecuniary; specific	Declare and participate
Julia Newton-Bishop	Department received payment from Roche for giving an introductory talk on the biology of melanoma.	Non-personal pecuniary; specific	Declare and participate
Julia Newton-Bishop	Received an honorarium from Roche for attending an advisory board meeting on the management of skin toxicity (April 2011).	Personal pecuniary; specific	Declare and participate
Julia Newton-Bishop	Received an honorarium from Roche for attending an advisory board meeting on the management of skin toxicity (July 2011).	Personal pecuniary; specific	Declare and participate
Julia Newton-Bishop	Department received payment from Roche for attending an advisory board meeting on the management of skin toxicity.	Personal pecuniary; specific	Declare and participate
Julia Newton-Bishop	Department received payment from Roche for making a training video on the management of skin toxicity.	Non-personal pecuniary; specific	Declare and participate

Julia Newton-Bishop	Department received payment from Roche for giving a talk on 'why do people get melanoma and what determines whether or not they survive' at the annual British Association of Dermatologists conference.	Non-personal pecuniary; specific	Declare and participate
Julia Newton-Bishop	Co-author on paper published in 2013 regarding the toxicity of vemurafenib.	Personal non-pecuniary	Declare and participate
Julia Schofield	Received a fee from Basilea for giving advice on their product toctino (treatment for hand eczema) into the marketplace.	Personal pecuniary; non-specific	Declare and participate
Julia Schofield	Received a fee and reimbursement of travel expenses from Leo Pharmaceuticals for giving a lecture on GPs with a special interest.	Personal pecuniary	Declare and participate
Julia Schofield	Received a fee and reimbursement of travel expenses from the British Dermatology Nursing Group for giving a lecture on dermoscopy and teledermatology in relation to skin cancer (including melanoma).	Personal pecuniary; specific	Declare and participate
Julia Schofield	Received a fee and reimbursement of travel expenses from the Dowling Club (national dermatology educational society) to present at a meeting for dermatology trainees on delivering dermatology services.	Personal pecuniary; non-specific	Declare and participate
Julia Schofield	Received a fee and reimbursement of travel expenses from the Primary Care Dermatology Society for presenting at a meeting on the management of pre-cancerous lesions in primary care.	Personal pecuniary; non-specific	Declare and participate

Julia Schofield	Received a fee and reimbursement of travel expenses from the Irish Primary Care Dermatology Society for presenting at a meeting on recognising skin lesions and paediatric dermatology problems.	Personal pecuniary;, non-specific	Declare and participate
Julia Schofield	During 2012, acted as an advisor to Buckinghamshire NHS Trust on redesigning their dermatology services.	Personal pecuniary; non-specific	Declare and participate
Julia Schofield	External advisor to All Party Parliamentary Group on Skin.	Personal non-pecuniary	Declare and participate
Julia Schofield	Trustee of the Psoriasis Association.	Personal non-pecuniary	Declare and participate
Julia Schofield	Received a fee and reimbursement of travel expenses from Leo Pharmaceuticals for giving a lecture on GPs with a special interest.	Personal pecuniary interest	Declare and participate
Julia Schofield	Received travel and subsistence from Conference Plus for giving a lecture to GPs in Namibia on non-melanoma skin cancer, eczema and topical dermatology.	Personal pecuniary	Declare and participate
Julia Schofield	Received a fee and reimbursement of travel expenses from the Irish Primary care Dermatology Society for giving talks on hyperhidrosis, skin lesion recognition and optimising primary/secondary care.	Personal pecuniary interest	Declare and participate
Laszlo Igali	Received a fee from St James' University Hospital, Leeds for speaking at a symposium on alopecia and immunohistochemistry in dermatopathology.	Personal pecuniary, non-specific	Declare and participate
Laszlo Igali	Received reimbursement of travelling expenses from the Royal College of Pathologists for attending a council meeting.	Personal pecuniary	Declare and participate

Laszlo Igali	Involved in the EUR-GAST II study (investigating environmental factors, H. pylori infection and genetic susceptibility in gastric cancer risk in the European population). Was the pathologist responsible for coordinating specimen collection and evaluation from the UK. No commercial funding.	Non-personal pecuniary; non-specific	Declare and participate
Laszlo Igali	Involved in the EPIC study. Did selective pathology data collection and evaluation. No commercial funding.	Non-personal pecuniary	Declare and participate
Laszlo Igali	Supervised an MSc student investigating optimal fixation of metastatic melanoma for tissue banking.	Non-personal pecuniary; specific	Declare and participate
Laszlo Igali	Involved in a new prospective study looking at BRAF immunostaining in metastatic melanoma to stratify patients for future treatment. Role is to do the immunohistochemistry and report on the BRAF status. Research funded by employer.	Non-personal pecuniary; specific	Declare and participate
Laszlo Igali	Ran a workshop on teledermatopathology as part of the American Society of Dermatopathology annual congress. No fee received for this activity.	Personal non-pecuniary	Declare and participate
Laszlo Igali	Holds the post of Editor of the Bulletin of the Royal College of Pathology.	Personal non-pecuniary	Declare and participate
Laszlo Igali	Provides ad-hoc advice to EZDerm on developing an integrated dermatology/ electronic record system. No fee received for this activity.	Personal non-pecuniary	Declare and participate

Laszlo Igali	Member of the Interim Body to the Professional Records Standard Body. Provides IT advice on how their electronic records should be set up.	Personal non-pecuniary	Declare and participate
Laszlo Igali	Received travelling expenses and accommodation from the British Association of Plastic, Reconstructive and Aesthetic Surgeons (BAPRAS) for giving a lecture at the Skin Cancer course on Basal cell carcinoma and squamous cell carcinoma, conventional and Mohs histology.	Personal pecuniary; non-specific	Declare and participate
Laszlo Igali	Treasurer for the professional record standard body (PRSB) for patient data standards.	Personal non-pecuniary	Declare and participate
Martin Telfer	Gave a presentation on 'Anatomical restrictions in the surgical excision of Scalp Sq CCa: does this effect local recurrence and regional nodal metastasis?' to the British Association of Oral and Maxillofacial Surgeons. No fee received.	Personal non-pecuniary	Declare and participate
Martin Telfer	Presented at the Yorkshire & Humber Regional Clinical Effectiveness Meeting on 'Facial skin cancer surgery: patient satisfaction'. No fee received.	Personal non-pecuniary	Declare and participate
Rachael Robinson	Received a fee from the RCGP for taking part in a panel reviewing a musculoskeletal e-learning package.	Personal pecuniary; non-specific	Declare and participate
Rachael Robinson	Received a fee from Galderma for chairing an educational meeting of the Leeds Skin Club on the treatment of acne and the red face.	Personal pecuniary; non-specific	Declare and participate

Rachael Robinson	Received reimbursement of travel expenses from the Yorkshire Deanery for attending a meeting to talk about the new curriculum for GP registrars.	Personal pecuniary; non-specific	Declare and participate
Rachael Robinson	Practice recruits patients into the 3C – cough complications cohort study, organised by Oxford University. Practice receives an income for this activity which is shared amongst the GPs.	Non-personal pecuniary; non-specific	Declare and participate
Rachael Robinson	Practice recruits patients into the early arthritis study, organised by Leeds University. Practice receives an income for this activity which is shared amongst the GPs.	Non-personal pecuniary; non-specific	Declare and participate
Rachael Robinson	Practice recruits patients into a study on transdermal patches for the treatment of chronic pain, organised by IMS Health. Practice receives an income for this activity which is shared amongst the GPs.	Non-personal pecuniary; non-specific	Declare and participate
Rachael Robinson	Currently involved in reviewing an acne decision aid tool for the BMJ patient decision aid group. No fee is being received.	Personal non-pecuniary non-specific	Declare and participate
Sara Stoneham	Received a fee from the Royal Marsden for giving a lecture on renal tumours in paediatric oncology as part of their MSc in Oncology.	Personal pecuniary; non-specific	Declare and participate
Sara Stoneham	Principal investigator for the CNS 9204 trial (Neuropsychological, academic and functional outcomes in survivors of infant ependymoma (UKCCSG CNS 9204)). Funded by CRUK. Not involved in designing the trial protocol.	Non-personal pecuniary non-specific	Declare and participate

Sara Stoneham	Was principal investigator for the GC 2005 04 (GC-3) trial (Protocol for the treatment of Extracranial Germ Cell Tumours in children and adolescents). Trial closed in 2009, 1 patient still in follow up. Sponsored by University Hospitals of Leicester NHS Trust. Funded by Children's Cancer and Leukaemia Group (CCLG).	Non-personal pecuniary; non-specific	Declare and participate
Sara Stoneham	Co-investigator in the HERBY trial (study of high grade paediatric glioma). Funded by Roche.	Non-personal pecuniary; non-specific	Declare and participate
Saskia Reeken	Received an honorarium from Leo Pharmaceuticals for attending an advisory board on dermatology (their psoriasis treatments and new products – none relating to melanoma).	Personal pecuniary, non-specific	Declare and participate.
Saskia Reeken	Received an honorarium from the British Dermatology Nursing Group for giving a lecture on topical treatments for dermatology (specifically steroid creams).	Personal pecuniary; non-specific	Declare and participate
Saskia Reeken	Received reimbursement of travel expenses (from the organiser) for attending the British Association of Dermatology Nursing annual conference.	Personal pecuniary; non-specific	Declare and participate
Saskia Reeken	Received a fee from Janssen for giving a lecture to dermatology nurses on the recognition of skin cancer lesions (including melanoma) in patients with psoriasis and the practical skills for lymph node examination.	Personal pecuniary; specific	Declare and withdraw from discussions on all topics regarding the recognition of melanoma until May 2013

Saskia Reeken	Received reimbursement of travel and subsistence expenses from the Danish Embassy in Copenhagen for attending a meeting on sun radiation and the effect on the environment.	Personal pecuniary; non-specific	Declare and participate
Saskia Reeken	Member of the CRUK Sun Smart Advisory Board – looks at strategies for sun awareness and health promotion.	Personal non-pecuniary	Declare and participate
Saskia Reeken	Member of the Melanoma Task Force – interested in improving the care of patients with melanoma.	Personal non-pecuniary	Declare and participate
Saskia Reeken	Nurse representative on the British Association of Dermatology skin cancer committee.	Personal non-pecuniary	Declare and participate
Saskia Reeken	Nurse representative on Skin Cancer UK – provides advice on skin cancer issues.	Personal non-pecuniary	Declare and participate
Saskia Reeken	Received sponsorship from LEO pharmaceuticals and Dermal Laboratories Limited for attending a study day on Maximising Capacity and Productivity in your Dermatology Service.	Personal pecuniary; non-specific	Declare and participate
Saskia Reeken	Received a practice development award of £900 from the British Dermatology Nursing Group. The award is to be used for professional development and will be put towards an MSc module of child health.	Personal pecuniary; non-specific	Declare and participate
Stephen Keohane	Received a fee from Meda for attending an advisory board on their new treatment for actinic keratosis (Zyclara).	Personal pecuniary; non-specific	Declare and participate
Stephen Keohane	Received a fee from Almirall for giving a lecture on new advances in non-melanoma skin cancer.	Personal pecuniary; non-specific	Declare and participate

Stephen Keohane	Received a fee from Leo Pharmaceuticals for attending an advisory board on their new treatment for actinic keratosis (Picato).	Personal pecuniary, non-specific	Declare and participate
Stephen Keohane	Received a fee from Roche for attending an advisory board on their treatment for advanced basal cell carcinoma (Erivedge).	Personal pecuniary; non-specific	Declare and participate
Stephen Keohane	Received reimbursement of expenses (travel, accommodation, subsistence and conference fee) from Leo Pharmaceuticals for attending the American Academy of Dermatology conference.	Personal pecuniary; non-specific	Declare and participate
Stephen Keohane	Local principal investigator for a trial on Ingenol (treatment of facial and scalp actinic keratoses). Trial is funded by Leo Pharmaceuticals. Responsible for administrating the trial locally. Not involved in designing the trial protocol.	Non-personal pecuniary; non-specific	Declare and participate
Stephen Keohane	Chaired a meeting on advanced melanoma management (content of the meeting was investigation and management and covered new therapeutic treatments including ipilimumab, vemurafenib, MEK inhibitors and DNA vaccines. The event was sponsored by Bristol Myers Squibb. Did not receive a fee or organise the meeting.	Personal non-pecuniary	Declare and participate
Stephen Keohane	Member of the National Cancer Intelligence Network Skin Reference Group – look at changing trends in skin cancer and how these impact on service provision.	Personal non-pecuniary	Declare and participate

Stephen Keohane	Chair of the British Association of Dermatologists Skin Cancer Committee – look at service provision and ensuring the quality of skin cancer care provided by dermatologists is equitable across the UK.	Personal non-pecuniary	Declare and participate
Stephen Keohane	Chair of the Skin Cancer Site Specific Group of the Central South Coast Cancer Network – look at local service provision and coordinate regional audits etc.	Personal non-pecuniary	Declare and participate
John Rouse	Member of the NCRI/AstraZeneca patient reference panel.	Personal non-pecuniary	Declare and participate
John Rouse	Received travelling expenses, subsistence allowance and overnight accommodation for a NCRI/AstraZeneca patient reference meeting at Alderley Park on 26 September 2013.	Personal pecuniary; non-specific	Declare and participate
John Rouse	Received travelling expenses, subsistence allowance and overnight accommodation from ESO and M-icab for attending a conference on Patient Participation in Melanoma Clinical Research.	Personal pecuniary; specific	Declare and participate
John Rouse	Received a bursary from the NCRN to attend the NCRI conference in Liverpool	Personal pecuniary	Declare and participate
John Rouse	Received travelling expenses, overnight accommodation and subsistence allowance paid for by CRUK for attending the NCRN/ECMC Combinations Alliance AZ Workshop.	Personal pecuniary	Declare and participate
John Rouse	Received travelling expenses costs from Macmillan Cancer support and accommodation costs from the meeting organisers for attending the Britain Against Cancer conference and Quality in Care awards.	Personal pecuniary	Declare and participate

Richard Jackson	Interviewed for the Daily Mail on the effectiveness of ipilimumab for metastatic melanoma.	Personal non-pecuniary	Declare and participate
Richard Jackson	Interviewed for the BBC on medical breakthroughs and the use of Ipilimumab received during treatment.	Personal non-pecuniary	Declare and participate
Richard Jackson	Photographed and filmed by Bristol-Myers Squibb Pharmaceuticals Ltd. Discussed his experience of metastatic melanoma. Film is to be used by BMS to make colleagues more aware of patients' unmet medical needs. No payment received.	Personal non-pecuniary	Declare and participate.
Julia Schofield	Received travel and accommodation costs from Conference Plus for giving a lecture in an educational programme for GPs. The lecture includes a session on skin lesion diagnosis.	Non-personal pecuniary; non-specific	Declare and participate
John Rouse	Received a bursary from the NCRN to attend the NCRI conference in Liverpool.	Personal pecuniary; non-specific	Declare and participate
John Rouse	Received travelling expenses, overnight accommodation and subsistence allowance paid for by CRUK for attending the NCRN/ECMC Combinations Alliance AZ Workshop.	Personal pecuniary; non-specific	Declare and participate
John Rouse	Received travelling expenses costs from Macmillan Cancer support and accommodation costs from the meeting organisers for attending the Britain Against Cancer conference and Quality in Care awards.	Personal pecuniary; non-specific	Declare and participate

Implementation: getting started

While developing this guideline, the Guideline Development Group identified 10 recommendations in 6 areas as key priorities for implementation. This section highlights 3 of those areas that could have a significant impact on practice and be challenging to implement. They have been identified with the help of stakeholders and members of the Guideline Development Group, using the criteria outlined in developing NICE guidelines: the manual, section 9.4. See 'Further resources' below for details of where to get help to address these challenges.

Challenge 1 – Using dermoscopy (dematoscopy) to assess pigmented lesions

See recommendation 1.2.1.

Potential benefits of implementation

Dermoscopy performed in secondary care by suitably trained specialists is both more sensitive and more specific in classifying skin lesions than clinical examination with the naked eye alone. It lessens the chance of missing a diagnosis of melanoma and reduces the number of unnecessary surgical procedures to remove benign lesions.

Challenges for implementation

For healthcare professionals in secondary care skin cancer clinics:

- Using dermoscopy routinely. Dermoscopy is integral to most dermatology services but is thought to be less commonly used in some clinics, for example clinics staffed by plastic and reconstructive surgeons.

For healthcare professionals who assess pigmented lesions:

- Developing competencies in assessment.
- Gaining experience in dermoscopy through regular practice.
- Including formal training in dermoscopy in their continuing professional development and revalidation work.
- Gaining access to new equipment (in some areas).

For relevant royal colleges and speciality training organisations:

- Including dermoscopy in speciality training curricula for healthcare professionals who assess pigmented lesions.

Making the changes happen

Commissioners of services could:

- Include provision of dermoscopy in local service specifications.

Providers of secondary skin cancer clinics could:

- Arrange for healthcare professionals who assess pigmented lesions to have formal training in dermoscopy. There are a range of academic institutions that deliver national and local courses.
- Routinely provide experiential training for staff in specialist clinics. This could include competency-based assessment.
- Include reference to ongoing experience and competency in the appraisals of healthcare professionals who perform dermoscopy.

The relevant royal colleges, supported by the speciality training organisations, could:

- Include dermoscopy where relevant in their speciality training curricula, and look at the General Medical Council's speciality training curriculum for dermatology as an example.
- Consider developing work-based assessments for measuring competency in the use of dermoscopy.

Challenge 2 – Measuring vitamin D levels and advising on supplementation

See recommendations 1.3.1 and 1.3.2.

Potential benefits of implementation

Measuring vitamin D levels at diagnosis allows healthcare professionals to identify people with melanoma whose vitamin D levels are low and who might benefit from supplementation in line with national policies, as well as people with high vitamin D levels who do not need supplementation and in whom supplementation might be harmful. Knowing a person's vitamin D level will also improve the accuracy of the advice given to them about the risks and benefits of sunlight exposure.

Challenges for implementation

For dermatologists (and possibly oncologists) in skin cancer multidisciplinary teams:

- Measuring vitamin D levels routinely at diagnosis of melanoma.
- Developing expertise in interpreting vitamin D levels.
- Providing advice about vitamin D supplementation if needed.

Making the changes happen

Dermatologists (and possibly oncologists) in skin cancer multidisciplinary teams could:

- Refer to the Scientific Advisory Committee on Nutrition for information on vitamin D supplementation.
- Refer to NICE's pathway on vitamin D: increasing supplement use among at-risk groups, which covers vitamin D supplementation in people with low or no exposure to the sun.
- Listen to the podcast produced by NICE to explain the evidence behind the recommendations on vitamin D and its supplementation.
- Use the Advice for melanoma health care teams – vitamin D and melanoma produced by GenoMEL (the Melanoma Genetics Consortium).

Challenge 3 – Considering sentinel lymph node biopsy and completion lymphadenectomy

See recommendations 1.5.2 and 1.7.1.

Potential benefits of implementation

Considering sentinel lymph node biopsy (SLNB) for people who have stage IB–IIC melanoma with a Breslow thickness of more than 1 mm, and discussing the possible advantages and disadvantages with them, will enable people with these melanomas to make an informed decision about whether or not to have this procedure. Those who choose to have SLNB may benefit from more accurate staging, giving a better indication of outcome (including survival and risk of relapse). SLNB is more sensitive than ultrasound, so lymphatic spread may be diagnosed earlier. In addition, people who have SLNB may be able to participate in clinical trials of new treatments.

Similarly, discussing the possible advantages and disadvantages of completion lymphadenectomy with people who have a positive SLNB will enable them to make an informed decision about whether or not to have this procedure after SLNB. Completion lymphadenectomy can reduce the chance of the melanoma returning and may enable the person to participate in clinical trials of new treatments.

Challenges for implementation

For clinicians in skin cancer multidisciplinary teams:

- Explaining the value of SLNB as a staging tool to people with melanoma, because there are no clear survival benefits from it.
- Providing comprehensive information about the possible advantages and disadvantages of having the procedure.
- Explaining the benefits of proceeding to completion lymphadenectomy to people with a positive SLNB result.

For commissioners:

- Providing SLNB in services.

Making the changes happen

Clinicians in skin cancer multidisciplinary teams could:

- Listen to the explanation of the evidence behind the SLNB recommendations on the NICE podcast.
- Use the option grids that NICE has produced to help discuss the possible risks and benefits of having SLNB and, for people with a positive SLNB, proceeding to completion lymphadenectomy.

Commissioners could:

- Ensure that service specifications include provision of SLNB. This may not be delivered locally.
- Visit the NICE local practice collection to see examples of SLNB services.

Further resources

Further resources are available from NICE that may help to support implementation.

NICE produces indicators annually for use in the Quality and Outcomes Framework (QOF) for the UK. The process for this and the NICE menu can be found here.

Uptake data about guideline recommendations and quality standard measures are available on the NICE website.

About this guideline

NICE clinical guidelines are recommendations about the treatment and care of people with specific diseases and conditions.

NICE guidelines are developed in accordance with a scope that defines what the guideline will and will not cover.

This guideline was developed by the National Collaborating Centre for Cancer, which is based at the Velindre NHS Trust in Cardiff. The Collaborating Centre worked with a Guideline Development Group, comprising healthcare professionals (including consultants, GPs and nurses), patients and carers, and technical staff, which reviewed the evidence and drafted the recommendations. The recommendations were finalised after public consultation.

The methods and processes for developing NICE clinical guidelines are described in the guidelines manual.

NICE produces guidance, standards and information on commissioning and providing high-quality healthcare, social care, and public health services. We have agreements to provide certain NICE services to Wales, Scotland and Northern Ireland. Decisions on how NICE guidance and other products apply in those countries are made by ministers in the Welsh government, Scottish government, and Northern Ireland Executive. NICE guidance or other products may include references to organisations or people responsible for commissioning or providing care that may be relevant only to England.

Strength of recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the Guideline Development Group is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

For all recommendations, NICE expects that there is discussion with the patient about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision (see also patient-centred care).

Interventions that must (or must not) be used

We usually use 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally we use 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions that should (or should not) be used – a 'strong' recommendation

We use 'offer' (and similar words such as 'refer' or 'advise') when we are confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. We use similar forms of words (for example, 'Do not offer…') when we are confident that an intervention will not be of benefit for most patients.

Interventions that could be used

We use 'consider' when we are confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Other versions of this guideline

The full guideline, melanoma: assessment and management of melanoma contains details of the methods and evidence used to develop the guideline. It is published by the National Collaborating Centre for Cancer.

The recommendations from this guideline have been incorporated into a NICE pathway.

We have produced information for the public about this guideline.

Implementation

Implementation tools and resources to help you put the guideline into practice are also available.

Your responsibility

This guidance represents the view of NICE, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when

exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summaries of product characteristics of any drugs.

Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

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