# Melanoma: assessment and management of melanoma

## NICE guideline

## Draft for consultation, January 2015

If you wish to comment on this version of the guideline, please be aware that all the supporting information and evidence is contained in the full version.

# Contents

# 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.

The incidence of melanoma is rising rapidly and is predicted to increase by 50% in the next 15 years. This is the fastest projected increase in incidence of any cancer.

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:

- diagnosing and staging melanoma, including the use of sentinel lymph node biopsy
- treating stages 0–4 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 vitamin D 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.

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 consultation, 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.

## 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.

## Key priorities for implementation

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

### *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.' **[1.1.1]**

## *Diagnosing melanoma*

### Dermoscopy and other visualisation techniques

- Assess all pigmented skin lesions that are referred for further assessment, and during follow-up, using dermoscopy carried out by healthcare professionals trained in this technique. **[1.2.1]**

### Photography

- For a clinically atypical melanocytic lesion that does not need excision at first presentation:
  - use baseline photography (preferably dermoscopic) **and**
  - review the clinical appearance of the lesion, using the baseline photographic images, 3 months after first presentation to identify early signs of melanoma. **[1.2.3]**

### Tumour samples for genetic testing

- If targeted systemic therapy is a treatment option for stage 4 disease, 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. **[1.2.7]**

## *Managing suboptimal vitamin D levels*

- Measure vitamin D levels at diagnosis in all people with melanoma. **[1.3.1]**

## *Staging investigations*

### Sentinel lymph node biopsy

- Consider sentinel lymph node biopsy as a staging rather than a therapeutic procedure for people with stage 1B–2C melanoma with a Breslow thickness of 1 mm or more, and give them detailed verbal and written information about the possible advantages and disadvantages, using the table below. **[1.5.2]**

| 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:<br>• around 1 out of 10 die within 10 years if the sentinel lymph node biopsy is negative<br>• 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 and this causes complications for 4–10 out of every 100 people who have the operation. |

## *Managing stage 3 melanoma*

### Completion lymphadenectomy

- Consider completion lymphadenectomy for people with a positive sentinel lymph node biopsy (stage 3A melanoma) and give them detailed verbal and written information about the possible advantages and disadvantages, using the table below **[1.7.1]**

| 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 more likely if the operation is in the groin than in other parts of the body. |
| 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. |

## *Follow-up after treatment for melanoma*

### Follow-up after stage 2C melanoma with no sentinel lymph node biopsy or stage 3 melanoma

- Consider surveillance imaging as part of follow-up for people who have had stage 2C melanoma with no sentinel lymph node biopsy or stage 3 melanoma and who would become eligible for systemic therapy as a result of early detection of metastatic disease if:
  - the specialist skin cancer multidisciplinary team agrees to a local policy and specific funding for imaging is identified **or**
  - there is a clinical trial of the value of regular imaging. **[1.9.15]**

# Stages of melanoma

The stages of melanoma used in this guideline are shown in the table below.

| Stage of melanoma | Description |
|---|---|
| 0 | In-situ melanoma that has not invaded the dermis |
| 1A | Breslow thickness less than 1 mm with no nodal or distant metastases |
| 1B | Breslow thickness less than 1 mm with ulceration or 1 or more mitoses, but no nodal or distant metastases |
| | Breslow thickness 1–2 mm with no ulceration or nodal or distant metastases |
| 2A | Breslow thickness 1–2 mm with ulceration but no nodal or distant metastases |
| | Breslow thickness 2–4 mm with no ulceration or nodal or distant metastases |
| 2B | Breslow thickness 2–4 mm with ulceration but no nodal or distant metastases |
| | Breslow thickness more than 4 mm with no ulceration or nodal or distant metastases |
| 2C | Breslow thickness more than 4 mm with ulceration but no nodal or distant metastases |
| 3A | Any Breslow thickness with no ulceration and micrometastases in 1 node at sentinel lymph node biopsy |
| | Any Breslow thickness with no ulceration and micrometastases in 2 or 3 nodes at sentinel lymph node biopsy |
| 3B | Any Breslow thickness with ulceration and micrometastases in 1–3 nodes at sentinel lymph node biopsy, with no distant metastases |
| | Any Breslow thickness but no ulceration and palpable metastasis to nodes confirmed histologically to be 1–3 in number |
| | Any Breslow thickness and in-transit metastases or microsatellites, but no ulceration, nodal or distant metastases |
| 3C | Any Breslow thickness and ulceration with palpable nodal metastases in up to 3 nodes or an in-transit or satellite lesion without palpable nodal metastases |
| | Any Breslow thickness, with or without ulceration, with palpable metastases in more than 4 nodes, matted nodes or in-transit metastases or satellite lesions, and a palpable nodal metastasis |
| 4 | Distant metastases in any organ, for example skin, nodes, internal organs or brain |

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 0–2C,

based on factors such as the thickness of the tumour and the presence or absence of ulceration (see table above). 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 3. 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 [hyperlink to be added for final publication] gives details of the methods and the evidence used to develop the guidance.

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 Diagnosing melanoma*

### Dermoscopy and other visualisation techniques

1.2.1 Assess all pigmented skin lesions that are referred for further assessment, and during follow-up, 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 lesions.

### Photography

1.2.3 For a clinically atypical melanocytic lesion that does not need excision at first presentation:

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

### Borderline and spitzoid melanocytic 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 tumour of unknown malignant potential on the basis of the histology, clinical features and behaviour.

1.2.6 Manage spitzoid tumours of unknown malignant potential as melanoma.

### Tumour samples for genetic testing

1.2.7 If targeted systemic therapy is a treatment option for stage 4 disease, 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 1A–2B primary melanoma at presentation except as part of a clinical trial.

1.2.9 Consider genetic testing of stage 2C primary melanoma or the nodal deposits or in-transit metastases for people with stage 3 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 3 melanoma.

## *1.3 Managing suboptimal vitamin D levels*

1.3.1 Measure vitamin D levels at diagnosis 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**

1.5.1 Do not offer imaging or sentinel lymph node biopsy for stage 1A or 1B melanoma with a Breslow thickness of less than 1 mm.

1.5.2 Consider sentinel lymph node biopsy as a staging rather than a therapeutic procedure for people with stage 1B–2C melanoma with a Breslow thickness of 1 mm or more, 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:<br>• around 1 out of 10 die within 10 years if the sentinel lymph node biopsy is negative<br>• 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 and this causes complications for 4–10 out of every 100 people who have the operation. |

**Imaging**

1.5.3 Offer CT staging to people with stage 3 or suspected stage 4 melanoma.

1.5.4 Include the brain as part of imaging for people with suspected metastatic disease.

1.5.5 Consider whole-body MRI for children and young people (from birth to 24 years) with stage 3 or suspected stage 4 melanoma.

## *1.6 Managing stages 0–2 melanoma*

### Excision

1.6.1 Consider excision with a clinical margin of at least 0.5 cm for people with stage 0 melanoma.

1.6.2 If an adequate histological margin is not achieved after excision for stage 0 melanoma, 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 1 (Breslow thickness less than 2 mm) melanoma.

1.6.4 Offer excision with a clinical margin of at least 2 cm to people with stage 2 (Breslow thickness 2 mm or more) melanoma.

### Imiquimod for stage 0 melanoma and skin metastases

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 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.

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

## *1.7 Managing stage 3 melanoma*

[1] At the time of consultation (January 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 consultation (January 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.

### Completion lymphadenectomy

1.7.1 Consider completion lymphadenectomy for people with a positive sentinel lymph node biopsy (stage 3A melanoma) 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 more likely if the operation is in the groin than in other parts of the body. |
| 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 for people with clinically detectable nodal disease

1.7.2 Offer therapeutic lymph node dissection to people with stage 3B–3C melanoma (those with clinically detectable nodal disease).

### Adjuvant radiotherapy

1.7.3 Do not offer adjuvant radiotherapy to people with stage 3A melanoma.

1.7.4 Do not offer adjuvant radiotherapy to people with stage 3B or 3C melanoma unless a reduction in the risk of local recurrence is estimated to outweigh the risk of significant adverse effects.

**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.

1.7.6 Offer surgery as a first option to people with isolated or limited in-transit metastases if local treatment is indicated.

1.7.7 If surgery or systemic treatment are not suitable for people with in-transit metastases, consider other local and regional treatment options, including:

- 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
- topical agents.

## *1.8 Managing stage 4 melanoma*

**Localised treatments for metastatic stage 4 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 the metastases.

**Localised treatment for 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 multidisciplinary team for a recommendation about treatment.

**Systemic anticancer therapy for unresectable or metastatic melanoma**

***Dabrafenib***

1.8.5 Refer to NICE's technology appraisal guidance on dabrafenib[3] for treating unresectable or metastatic BRAF V600 mutation-positive melanoma for adults.

***Dacarbazine***

1.8.6 Consider dacarbazine[4] for people with stage 4 metastatic melanoma if immunotherapy or targeted therapy are not suitable.

1.8.7 Do not offer further cytotoxic chemotherapy for stage 4 metastatic melanoma to people previously treated with dacarbazine except in the context of a clinical trial.

***Ipilimumab***

1.8.8 For adults, 'Ipilimumab[5] is recommended as an option for treating advanced (unresectable or metastatic) melanoma in people who have received prior therapy, only if the manufacturer provides ipilimumab with the discount agreed in the patient access scheme'. [This recommendation is from NICE's technology appraisal guidance on ipilimumab for previously treated advanced (unresectable or metastatic) melanoma.]

[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] Although this use is common in UK clinical practice, at the time of consultation (January 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.
[5] Ipilimumab has a UK marketing authorisation 'for the treatment of advanced (unresectable or metastatic) melanoma in adults'.

1.8.9 Refer to NICE's technology appraisal guidance on ipilimumab[6] for previously untreated advanced (unresectable or metastatic) melanoma for adults.

***Vemurafenib***

1.8.10 For adults, 'Vemurafenib[7] 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'. [This recommendation is from NICE's technology appraisal guidance on vemurafenib for treating locally advanced or metastatic BRAF V600 mutation-positive malignant melanoma.]

## *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 Include the brain for people having imaging as part of follow-up or when metastatic disease is suspected.

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

1.9.5 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 when metastatic disease is suspected.

[6] Ipilimumab has a UK marketing authorisation 'for the treatment of advanced (unresectable or metastatic) melanoma in adults'.
[7] Vemurafenib has a UK marketing authorisation for 'the treatment of adult patients with BRAF V600 mutation-positive unresectable or metastatic melanoma'.

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

1.9.7 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 and vitamin D (in line with recommendation 1.1.3), and NICE guidance on smoking cessation.

1.9.8 Continue to manage concurrent drug treatment in line with recommendations 1.4.1 and 1.4.2.

**Follow-up after stage 0 melanoma**

1.9.9 Discharge people who have had stage 0 melanoma after completion of treatment and provide advice in line with recommendation 1.9.7

**Follow-up after stage IA melanoma**

1.9.10 For people who have had stage 1A melanoma, consider follow-up 2–4 times during the first year after completion of treatment and discharging them at the end of that year.

1.9.11 Do not routinely offer screening investigations (including imaging and blood tests) as part of follow-up to people who have had stage 1A melanoma.

**Follow-up after stages 1B–2B melanoma or stage 2C melanoma (fully staged using sentinel lymph node biopsy)**

1.9.12 For people who have had stages 1B–2B melanoma or stage 2C 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.

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

stages 1B–2B melanoma or stage 2C melanoma with a negative sentinel lymph node biopsy.

**Follow-up after stage 2C melanoma with no sentinel lymph node biopsy or stage 3 melanoma**

1.9.14 For people who have had stage 2C melanoma with no sentinel lymph node biopsy, or stage 3 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.

1.9.15 Consider surveillance imaging as part of follow-up for people who have had stage 2C melanoma with no sentinel lymph node biopsy or stage 3 melanoma and who would become eligible for systemic therapy as a result of early detection of metastatic disease if:

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

**Follow-up after stage 4 melanoma**

1.9.16 Offer personalised follow-up to people who have had stage 4 melanoma.

# 2 Implementation: getting started

NICE has worked with the Guideline Development Group to identify the recommendations in this draft guideline that may have the largest impact on practice or be the most challenging to implement. If the draft recommendations are not changed after consultation we think that the most important and challenging recommendations to implement will be in these 3 areas:

- dermoscopy to assess pigmented lesions (recommendation 1.2.1)
- vitamin D measurement and supplementation (recommendations 1.3.1 and 1.3.2)

- sentinel lymph node biopsy as a staging rather than a therapeutic procedure (recommendation 1.5.2).

## *How stakeholders can help us with implementation*

During consultation we would like stakeholders to let us know if you agree with these choices, or if you would choose recommendations in other areas of the draft guideline. We would also like you to send us suggestions for ways of addressing the challenges to implementation – such as sharing examples of good practice, or highlighting existing educational materials or other resources. We will use your responses to create a targeted implementation section in the final guideline.

Please send us your comments and suggestions using the comments form.

## *Challenges for implementation*

### Dermoscopy (recommendation 1.2.1)

The draft guideline recommends that clinicians should use dermoscopy to assess all pigmented skin lesions referred for further assessment and during follow-up and that they should have had formal training in this technique.

The use of dermoscopy to assess pigmented lesions varies across the country. The implementation challenge would be to ensure that dermoscopy is used consistently throughout secondary care. New equipment would be needed, and healthcare professionals who assess pigmented lesions, including dermatologists, oncologists and GPs with a special interest, may need formal training in dermoscopy as part of their specialist training and revalidation.

### Vitamin D (recommendations 1.3.1 and 1.3.2)

The draft guideline recommends measuring vitamin D levels at diagnosis in everyone with melanoma and offering advice about supplementation to people whose levels are thought to be suboptimal.

Very few skin cancer multidisciplinary teams (MDTs) currently measure vitamin D levels in people diagnosed with melanoma. Recognising suboptimal

vitamin D levels and giving advice on supplementation and monitoring would be a significant change to current practice. There is a lack of consensus among healthcare professionals about optimal vitamin D levels in the general population and about the significance of the low levels commonly found in the UK. This has led to uncertainty about whether to measure vitamin D levels and whether supplementation should be offered to people with melanoma.

Dermatologists (and possibly oncologists) in melanoma clinics would need to start measuring vitamin D levels routinely when melanoma is diagnosed. They would also need to develop expertise in interpreting the significance of vitamin D measurements and providing advice about supplementation if needed.

**Sentinel lymph node biopsy (recommendation 1.5.2)**

The draft guideline recommends that sentinel lymph node biopsy be considered as a staging rather than a therapeutic procedure for people with stage 1B–2C melanoma with a Breslow thickness of 1 mm or more, after giving them detailed information about the possible advantages and disadvantages.

Currently 45% of skin cancer MDTs do not offer sentinel lymph node biopsy. Doctors and nurses in these MDTs may need to become better informed about the value of this procedure as a staging tool because there are no clear survival benefits from it. In units where sentinel lymph node biopsy is already an integral component of the melanoma service, the skin cancer MDT would need to ensure that they provide comprehensive information about the possible risks and benefits of having the procedure for staging purposes to people with melanonoma who may be offered it. This may necessitate changes in the extent of the information provided to people and the time allocated for discussion. Sentinel lymph node biopsy may also need to be provided in services that do not currently offer it.

# 3 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.

## *3.1 Techniques for confirming a diagnosis in people with suspected atypical spitzoid melanocytic lesions*

In people with reported atypical spitzoid melanocytic 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**

Borderline and 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.

## *3.2 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.

## *3.3 Follow-up surveillance imaging*

In people treated for high-risk stage 2 and 3 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.

## *3.4 Vitamin D supplementation*

In people with stage 1–3 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 protect against melanoma-related death. 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.

## *3.5 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.

# 4 Other information

## *4.1 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 5), which reviewed the evidence and developed the recommendations.

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

## *4.2 Related NICE guidance*

Details are correct at the time of consultation on the guideline (January 2015). 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
- Improving supportive and palliative care for adults with cancer (2004) NICE guideline CSGSP

***Condition-specific***

- 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
- Skin tumours including melanoma (2010) NICE guideline CSGSTIM

**Under development**

NICE is developing the following guidance:

- Suspected cancer. NICE guideline. Publication expected May 2015
- Sunlight exposure – benefits and risks. NICE guideline. Publication expected July 2015
- Skin cancer: the VivaScope 1500 and 3000 systems for detecting and monitoring skin lesions. NICE diagnostics guidance. Publication expected November 2015
- Melanoma (BRAF V600E mutation- positive, unresectable, metastatic) – dabrafenib and trametinib. NICE technology appraisal guidance. Publication date to be confirmed

- Melanoma (resected stage 4, high risk stage 3) – ipilimumab (adjuvant). NICE technology appraisal guidance. Publication date to be confirmed

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

## *5.1 Guideline Development Group*

**Gill Godsell**

Skin Cancer Clinical Nurse Specialist, Nottingham University Hospitals NHS Trust

**Lazslo Igali**

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, Newcastle

**Stephen Keohane**

Consultant Dermatologist, Portsmouth Hospitals NHS Trust, Portsmouth Dermatology Centre

**Fergus Macbeth**

Clinical advisor, Wales Cancer Trials Unit, Cardiff University

**Julia Newton Bishop**

Professor of Dermatology, University of Leeds

**Christine Parkinson**

Consultant in Medical Oncology, Addenbrookes Hospital, Cambridge

**Barry Powell**

Consultant Plastic Surgeon, St George's Hospital, London

**Saskia Reeken**

Clinical Nurse Specialist, Skin Cancer & Dermatology, Kingston Hospital NHS Trust, Surrey

**Rachael Robinson**
GP and GPSI Dermatology, Stockwell Road Surgery, Knarlesborough

**John Rouse**
Patient and carer member

**Julia Schofield**
Consultant Dermatologist, United Lincoln 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

## *5.2 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

**Angharad Morgan**
Researcher

**Delyth Morris**
Information Specialist

**Susan O'Connell**
Researcher

**Matthew Prettyjohns**
Senior Health Economist

## *5.3 NICE project team*

**Christine Carson**
Guideline Lead

**Mark Baker**
Clinical Adviser

**Katie Perryman Ford**
Guideline Commissioning Manager

**Jennifer Watson-Henry**
Guideline Coordinator

**Nichole Taske**
Technical Lead

**Bhash Naidoo**
Health Economist

**Judy McBride**
Editor

## *5.4 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.

| 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 | Personal Pecuniary Interest, | Declare and participate |

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| | Boehringer Ingelheim for attending the International Gynaecological Cancer Society conference. | Non-specific | |
| 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 | Personal pecuniary; | Declare and participate |

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| | expenses from CLOVIS for attending an investigator meeting for the ARIEL2 and ARIEL3 trials for ovarian cancer. | non-specific | |
| 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. Give 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 | Non-specific | Declare and participate |

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| | RCT multi-centre trial in drug therapy for metastatic renal cell cancer. | | |
| 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 | Research funds received an honorarium 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 | Personal pecuniary; non-specific | Declare and participate |

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| | data collection on skin cancer. | | |
| 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. | 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. | 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 | Non-personal pecuniary; | Declare and participate |

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| | the management of skin toxicity. | specific | |
| 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 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 | Personal pecuniary; non-specific | Declare and participate |

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| | Care Dermatology Society for presenting at a meeting on the management of pre-cancerous lesions in primary care. | | |
| 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 |
| 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 | Non-personal pecuniary | Declare and participate |

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| | funding. | | |
| 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 |

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| 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 |

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| 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. |

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| 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 in 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 | Personal pecuniary; non-specific | Declare and participate |

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| | in your Dermatology Service. | | |
| 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 (Everidge). | 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 | Personal Non- | Declare and participate |

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| | 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. | Pecuniary | |
| 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 co-ordinate 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 | Personal pecuniary; specific | Declare and participate |

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| | conference on Patient Participation in Melanoma Clinical Research. | | |
| Richard Jackson | Interviewed for the Daily Mail on the effectiveness of ipilimumab for metastatic melanoma. | Personal non-pecuniary | Declare and participat |
| Julia Schofield | Received travel and accommodation costs from Conference Plus for a giving a lecture in an educational program for GPs. The lectures will include 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 |