GUIDELINES

Melanoma: summary of NICE guidance

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This is one of a series of BMJ summaries of new guidelines based on the best available evidence; they highlight important recommendations for clinical practice, especially where uncertainty or controversy exists.

Further information about the guidance, a list of members of the guideline development group, and the supporting evidence statements are in the full version on thebmj.com.

Melanoma is the fifth most common cancer in the United Kingdom, with more than 13 000 cases diagnosed in 2011 and its incidence is rising rapidly.[1] Clinical practice seems to vary in the UK, especially with regard to the use of dermoscopy and photography, access to sentinel lymph node biopsy, vitamin D measurement and advice, follow-up policies, and the use of routine follow-up imaging. Patient groups have reported inadequate information on management options.

This article summarises the most important recent recommendations from the National Institute for Health and Care Excellence (NICE) on the diagnosis and care of people with melanoma.[2]

Recommendations

NICE recommendations are based on systematic reviews of the best available evidence and explicit consideration of cost effectiveness. When minimal evidence is available, recommendations are based on the guideline development group's experience and opinion of what constitutes good practice. Evidence levels for the recommendations are in the full version of this article on bmj.com. The recommendations specifically apply to secondary and tertiary care locations, where these patients should all be managed by specialist multidisciplinary teams (MDTs), but they will also affect the management of patients with melanoma in primary care.

The staging of melanoma is detailed and complex and the full staging system is available online.[3] The brief explanations of stage given may not be precise and are there to help make the context of the recommendation clearer.

AMELIE-BENOIST/SPL

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

Committee members involved in this guideline update included lay members who contributed to the formulation of the recommendations summarised here. Patient and carer organisations were among the stakeholders who commented on the draft guideline.

THE BOTTOM LINE

- Use dermoscopy to examine all pigmented lesions referred for assessment and ensure that all staff are adequately trained in its use
- Consider sentinel node biopsy as a staging tool for patients with stage II melanoma and stage 1B melanoma thicker than 1 mm. Use box 1 or the options grid being developed to discuss the potential advantages and disadvantages of the procedure with patients
- If a sentinel node biopsy is positive for melanoma, discuss the potential advantages and disadvantages of completion lymphadenectomy with the patient using box 2 or the options grid being developed
- Consider regular imaging in patients at greater risk of progression to stage IV (metastatic) melanoma. Use box 3 or the options grid being developed to discuss potential advantages and disadvantages of this with the patient

Communication and support

- To help people make decisions about their care, follow the recommendations on communication, information provision, and support in the NICE guideline on improving outcomes for people with skin tumours including melanoma.[4]

Assessing melanoma

- Assess all pigmented skin lesions that are referred for assessment or identified during follow-up using dermoscopy carried out by healthcare professionals trained in this technique. Do not routinely use confocal microscopy or computer assisted diagnostic tools.

Photography

- For a clinically atypical melanocytic lesion that does not need excision at first presentation use baseline photography (preferably dermoscopic). Also use this technique to review the clinical appearance of the lesion three months after first presentation to identify early signs of melanoma.

Box 1 | Possible advantages and disadvantages of sentinel lymph node biopsy (SLNB)

Advantages	Disadvantages
SLNB helps to find out whether the cancer has spread to the lymph nodes and is better than ultrasound scans at finding very small cancers in the lymph nodes	The purpose of SLNB is not to cure the cancer. There is no good evidence that people who have the operation live longer than those who do not have it
It can help predict what might happen in the future. For example, in people with a 1-4 mm thick primary melanoma, about one in 10 dies within 10 years if SLNB is negative; about three in 10 die if SLNB is positive	The result needs to be interpreted with caution. For every 100 people with a negative SLNB result, about three will develop a recurrence in the same group of lymph nodes
People who have had SLNB 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	The operation requires a general anaesthetic
	The procedure results in complications such as deep venous thrombosis, seromas, or wound infections in 4-10 of every 100 people

Box 2 | Possible advantages and disadvantages of completion lymphadenectomy

Advantages	Disadvantages
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; it is more 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 four out of five 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 those who do not have it
	Having any operation can cause complications

Box 3 | Possible advantages and disadvantages of follow-up imaging

Advantages	Disadvantages
Early detection of recurrence may allow people to receive treatment with drugs such as immunotherapeutic agents earlier than they would otherwise, which might lead to better outcomes	There is currently no evidence that treating recurrent melanoma earlier increases the probability of a better outcome
Some patients find it reassuring to have regular scans	Having regular scans may increase some people's anxiety, even though for many, no recurrence will ever occur
	Regular scans increase the body's exposure to radiation, which itself increases the risk of second cancers later in life. For example, imaging of the chest results in a very small increase in the risk of thyroid cancer
	Imaging of the brain and neck results in a small increase in the risk of developing cataracts
	Incidental abnormalities of no clinical significance that require further investigations might be identified, and this may cause anxiety until the situation is resolved

Taking tumour samples for genetic testing

With the advent of effective treatments for people with metastatic disease, genetic testing of tumour samples for driver mutations (such as *BRAF*), which determine the likelihood of response to therapy, is becoming more important. For those who are being considered for systemic therapy:

- Offer genetic testing using a secondary (metastatic) melanoma tissue sample or a primary melanoma tissue sample if a secondary sample is not available or is of inadequate cellularity.

However:

- Do not offer genetic testing of stages IA-IIB primary melanoma (≤4 mm thick with ulceration or >4 mm thick with no ulceration, no spread) at presentation except as part of a clinical trial.
- For stage IIC primary melanoma (>4 mm thick, no spread, ulcerated), consider genetic testing.
- For stage III melanoma (spread to lymph nodes or the cutaneous or subcutaneous lymphatics proximal to those nodes—"in transit" metastases), consider testing metastatic tissue; if insufficient material is available, genetic testing of the primary tumour may be necessary.

Managing suboptimal vitamin D levels

Many people with melanoma have suboptimal levels of vitamin D at diagnosis but are usually advised to avoid sun exposure to reduce the risk of further melanomas. Vitamin D is important for bone health and possibly for other aspects of health, so further reduction in levels should be avoided. The guideline also suggests avoiding high levels as a result of unnecessary supplementation.

- Measure vitamin D levels at diagnosis in all people with melanoma.
- For people whose vitamin D levels are thought to be suboptimal, provide advice on supplementation and monitoring in line with local policies and the NICE guideline on vitamin D.[5]

Staging investigations

The role of sentinel lymph node biopsy (SLNB) is controversial, with its routine use varying greatly across England and Wales. Not all people routinely need imaging at diagnosis:

- Do not offer imaging or SLNB to people who have stage I melanoma with a Breslow thickness of 1 mm or less.
- Consider SLNB as a staging rather than a therapeutic procedure for people with stages IB-IIC melanoma with a Breslow thickness of more than 1 mm, and give these people detailed verbal and written information about the possible advantages and disadvantages (see box 1).
- Offer computed tomography staging to people with stage IIC melanoma who have not had SLNB and to people with stage III (lymph nodes or in transit spread) or suspected stage IV melanoma (distant metastases). Include imaging of the brain for people with suspected stage IV melanoma.
- Consider whole body magnetic resonance imaging for children and young people (from birth to 24 years) with stage III or suspected stage IV melanoma.

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- Suspected cancer (part 1—children and young adults) (*BMJ* 2015;350:h3036)
- Suspected cancer (part 2—adults) (*BMJ* 2015;350:h3044)
- Management of anaemia in chronic kidney disease (*BMJ* 2015;350:h2258)
- Bronchiolitis in children (*BMJ* 2015;350:h2305)
- Challenging behaviour and learning disabilities (*BMJ* 2015;350:h2652)

Managing stages 0-II melanoma

With regard to excision margins:

- Consider a clinical margin of at least 0.5 cm when excising stage 0 melanoma (in situ), but if excision does not achieve an adequate histological margin, discuss further management with the MDT.
- Offer excision with a clinical margin of at least 1 cm to people with stage I (≤2 mm thick) and of at least 2 cm to people with stage II melanoma (1.01-2 mm thick if ulcerated or >2 mm thick).

Managing stage III melanoma (lymph nodes or in transit spread)

There is controversy and practice variation about the management of involved lymph nodes found at SLNB, by imaging, or at clinical examination.

- Consider completion lymphadenectomy (removing residual local lymph nodes) for people whose SLNB shows micrometastases and give them detailed verbal and written information about the possible advantages and disadvantages (see box 2).
- Offer therapeutic lymph node dissection to people with palpable stages IIIB-IIIC nodal melanoma or nodal disease detected by imaging.
- Do not offer adjuvant radiotherapy to people with stage IIIA disease or to those with stage IIIB or IIIC melanoma unless a reduction in the risk of local recurrence is estimated to outweigh the risk of serious adverse effects.

Managing stage IV melanoma (distant metastases)

Many patients with metastases will be treated with targeted therapy in line with NICE guidance on dabrafenib, ipilimumab and vemurafenib.[6-9] However, some situations require separate advice:

- Refer the care of people with oligometastases (metastases of limited extent, for which ablation or surgery may be feasible) to the specialist skin cancer MDT for recommendations about staging and management.
- Consider surgery or other ablative treatments (including stereotactic radiotherapy or radioembolisation) to prevent and control symptoms in consultation with site specific MDTs (such as MDTs for the brain or bones).
- Discuss the care of people with melanoma and brain metastases with the specialist skin cancer MDT.
- 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.

Cytotoxic chemotherapy may be indicated for patients who are unsuitable for targeted systemic therapies:

- Consider dacarbazine for people with stage IV metastatic melanoma if immunotherapy or targeted therapy is not suitable.
- 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.

Follow-up after treatment for melanoma

- All local follow-up policies should include reinforcing advice about self examination as well as health promotion for people with melanoma and their families, including sun awareness while avoiding vitamin D depletion (in line with local policies and the NICE guideline on vitamin D),[5] and smoking cessation.
- Discharge people who have had stage 0 melanoma after completing treatment.
- For those with stage IA melanoma (≤1 mm thick, no spread, no ulceration, no mitoses), consider follow-up two to four times during the first year after completing treatment and discharge at the end of that year. Do not routinely offer screening investigations (including imaging and blood tests) as part of follow-up.
- For those with stages IB-IIB melanoma (any thickness if not ulcerated, up to 4 mm thick if ulcerated, no spread) or stage IIC melanoma (>4 mm thick, ulcerated, no spread) with a negative SLNB, consider follow-up every three months for the first three years after completing treatment, then every six months for the next two years and discharge at the end of five years. Do not routinely offer screening investigations (including imaging and blood tests) as part of follow-up.
- For people who have had stage IIC melanoma but no SLNB or stage III (involved lymph nodes) melanoma, consider follow-up every three months for the first three years after completion of treatment, then every six months for the next two years, and discharge at the end of five years.
- For people who have had stage IIC melanoma, but no SLNB, or stage III melanoma, and who would become eligible for systemic therapy as a result of early detection of metastatic disease, consider surveillance imaging as part of follow-up if there is a clinical trial of the value of regular imaging or if the specialist skin cancer MDT agrees to a local policy and specific funding for imaging six monthly for three years is identified. Discuss the possible advantages and disadvantages of surveillance imaging (box 3) with the person.
- For people who have had stage IV (distant metastases) melanoma, offer personalised follow-up.

Overcoming barriers

Dermoscopy is not routinely used in all clinics where pigmented lesions are assessed, so equipment will need to be purchased and staff trained. Vitamin D is rarely measured and there is uncertainty about how best to manage suboptimal levels. New guidance from the Scientific Advisory Committee on Nutrition (SACN) expected in 2015 will be helpful. Not all MDTs offer SLNB and some that do reportedly do not always offer the choice of not having it. Change is needed both in how this is discussed with patients and in its provision where it is currently unavailable.

CPD/CME

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SUMMARIES OF BMJ CLINICAL EVIDENCE

Ear wax

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This series comprises summaries of BMJ Clinical Evidence, a database of systematic overviews of the best available evidence on the effectiveness of commonly used interventions (available at http://clinicalevidence.bmj.com/).

Ear wax only becomes a problem if it causes a hearing impairment or other ear related symptoms. The accumulation of wax occurs for many different reasons, including overproduction or underproduction of its constituent components, a failure to self clear because of slow skin migration, or mechanical issues such as the use of cotton buds or hearing aids. Wax may obscure the view of the tympanic membrane and may need to be removed for diagnostic reasons or for taking impressions before fitting a hearing aid or making ear plugs.

If wax needs to be removed, there are various options available. These include: irrigation (syringing); the use of wax softeners or solvents alone; the use of wax softeners before irrigation; and the manual removal of wax by use of an oto-endoscope and small instruments or a binocular microscope with suction and micro instruments. Irrigation relies on getting water past the wax in the ear canal, so that it builds up deep to the wax and then pushes it outwards. Thus, if the wax is completely occluding the canal, this technique can easily make matters worse by impacting the wax against the tympanic membrane. If there are pre-existing changes to the tympanic membrane, damage can occur; so there are many contraindications to irrigation. Oto-endoscopes give only a monocular view of the ear canal, and practice is needed with instrumentation to become competent at wax removal without trauma. Binocular microscopes give a stereoscopic view and are probably the safest way of dewaxing an ear, especially when suction is used, but they are expensive and users need training.

Evidence for the effects of methods to remove ear wax

Effects	Treatment
Trade-off between benefits and harms	
Clinicians and patients should weigh up beneficial and harmful effects according to individual circumstances and priorities	Ear irrigation (syringing)—considered to be effective, but may be associated with adverse effects*
Unknown effectiveness	
Data are currently insufficient or of inadequate quality	Manual removal (other than ear irrigation)
	Wax softeners before irrigation
	Wax softeners alone

*Although we found no randomised controlled trials, there is consensus that irrigation is effective at removing ear wax.

THE BOTTOM LINE

- Ear wax only needs to be removed if it causes hearing impairment, other symptoms, or if view of the tympanic membrane is required for diagnostic reasons or for taking impressions for hearing aids or ear plugs
- Ear irrigation (syringing) is generally considered to be effective, but evidence is limited and it may be associated with adverse effects
- There are insufficient data on other mechanical methods of wax removal or on use of wax softeners to draw robust conclusions on their effectiveness

Key findings: efficacy of interventions

The table lists the evidence for the effects of methods to remove ear wax.

Clinical guide to treatments

- For such a commonly occurring condition, there is little high quality evidence available to guide practice.
- All procedures for removing wax should be essentially pain-free.
- Ear irrigation (syringing): This is generally considered to be effective, but evidence is limited.[1] Irrigation is usually performed using a motorised pump with a governable pressure. Syringing with unregulated manual syringes should no longer be used.
- Ear irrigation may be associated with vertigo and tympanic membrane perforation in some people. Pain, damage to the skin of the ear canal, and otitis externa are other possible adverse effects.[2] Ear irrigation may rarely cause permanent deafness; therefore, people with hearing in only one ear should not have this ear irrigated.[2] A history of ear disease or ear surgery is also a contraindication.[2]
- Manual removal (other than ear irrigation), including other mechanical methods of removing ear wax by staff trained in the use of specific instruments such as microsuction, is probably effective, although the evidence is limited.[1] Mechanical removal of wax with suction, probes, or forceps is considered effective, but it can cause trauma to the ear canal, depending on the experience and training of the operator and the ease of view.
- Wax softeners: Overall, we found limited high quality evidence on the effects of proprietary wax softeners.[1]
  - With regard to the use of wax softeners before irrigation, we found very weak evidence that wax softeners may be better than no treatment. However, we found no good evidence that wax softeners improved wax clearance after irrigation compared with saline.[1] We found no good evidence that any one type of wax softener was better than any other for use before irrigation.[1]
  - With regard to the use of wax softeners alone, we found very weak evidence that wax softeners may be better than no treatment.[1] We found no consistent evidence that wax softeners alone improved wax clearance compared with sterile water or normal saline. We found no good evidence that any one type of wax softener alone was better than any other.[1]
- Overall, many of the included randomised controlled trials had weak methods, which limited the robustness of any conclusions that could be drawn.