The incidence of all types of skin cancers is increasing. Nonmelanoma skin cancer (NMSC) is the most common group of cancers, accounting for roughly 20% of all new malignancies and 90% of all skin cancers registered in the UK and Ireland. NMSCs are most common in older men, with sun exposure being the most significant risk factor. Common places for NMSC to occur are sun-exposed body parts, such as the face, neck, ears, forearms and hands. Over 80% of tumours occur in these sites. While most NMSC are rarely fatal, they can result in considerable morbidity and present an increasing burden on healthcare services.

Different types of nonmelanoma skin cancer
The two major types of NMSC are basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). BCC represents about 74% of NMSCs and SCC 23%. The remaining NMSCs include a variety of rare tumours, such as dermatofibrosarcoma protuberans (DFSP) and Merkel cell carcinomas. Awareness of less common tumours is important to avoid misdiagnosis and mismanagement.

Size of the problem and impact on healthcare resources
The incidence of NMSC is under-reported in the UK due to inconsistent data collection, which makes estimating the real size of the problem difficult. Data collection inaccuracies also limit more detailed analysis of the factors underlying the wide regional variations in incidence of NMSC. Despite these recording inconsistencies, there does appear to be a true increase in NMSC incidence, which has occurred fairly rapidly. This is estimated to be a 30% increase in the last decade. This parallels with increases in other types of skin cancer, such as in melanoma, suggesting that rising numbers are genuine rather than just related to improvements in data collection.

In 2014, there were 131,772 cases of NMSC registered in the UK: 73,925 (56%) in males and 57,847 (44%) in females, giving a male: female ratio of around 7:5. The crude incidence rate shows that there are 233 new NMSC cases for every
100,000 males in the UK and 176 for every 100,000 females. The management of NMSC imposes a significant workload on both primary and secondary care services. The burden of skin lesion management in dermatology outpatient services is also great, with 35–45% of specialist referrals relating to the diagnosis and management of skin lesions. This figure is as high as 60% in some regions. Furthermore, approximately 88% of two-week wait urgent referrals for suspected skin cancer result in a nonmalignant diagnosis. This illustrates the difficulties of accurate skin lesion diagnoses and highlights the need for more training in primary care and the development of newer referral models, eg teledermatology, to reduce unnecessary referrals.

Clinical presentations

Basal cell carcinomas

BCCs or ‘rodent ulcers’ rarely metastasise and almost never result in mortality; however, they can erode local anatomical structures, particularly on the head and neck. There are different subtypes of BCC, which have different clinical presentations. There are broadly five different types: nodular, superficial, infiltrative, pigmented and basosquamous. A combination of these types may occur.

Nodular basal cell carcinoma

Nodular BCC is the most common subtype, accounting for approximately 50% of all BCCs. Lesions typically present as a shiny, pearly papule or nodule with a smooth surface and the presence of arborising telangiectasias. With time, the tumour can enlarge and ulcerate but an elevated pearly rolled border usually remains (see Figure 1). Common sites are the face, especially the cheeks, nasolabial folds, forehead and eyelids. Nodular BCCs may arise in any hair-bearing area of the skin but are rarely seen in nonhair-bearing sites, eg genital mucosa.

The clinical differential diagnosis of nonulcerated lesions includes adnexal neoplasms, intradermal melanocytic nevi, Merkel cell carcinoma and cutaneous amelanotic melanoma.

Superficial BCCs

Superficial BCCs (sBCC; see Figure 2) typically present as a well-circumscribed, erythematous macule, which can be scaly or crusted. They can be often incorrectly diagnosis as eczema or psoriasis. The clinician should be wary of single or multiple scaly patches on the back that are not itchy. The diameter can vary from a few millimetres to several centimetres.

They are more common in a younger age group than other types of BCC. They favour the trunk and extremities, and less often occur in the head and neck region. Multiple lesions may be present. The clinical differential diagnosis includes solitary lichenoid keratosis and Bowen’s disease as well as inflammatory diseases such as psoriasis, eczema and cutaneous lupus erythematosus.

Infiltrative or morphoeic basal cell carcinoma

This less common subtype of BCC frequently presents as a much more subtle light pink or white area that can resemble a scar. The surface of the lesion is typically smooth, although crusts with underlying erosions or ulcerations do occur. An ele

Figure 1. Nodular basal cell carcinoma (BCC) typically presents as a shiny, pearly papule or nodule with a smooth surface and the presence of arborising telangiectasias.

vated pearly border is typically absent. The biological behaviour is usually more aggressive, with extensive local destruction.

Pigmented BCC

Pigmented BCCs are seen more often in darker skinned persons such as Latin Americans and Asians. This subtype has all the characteristics of the nodular-ulcerative variety plus brown or black pigmentation and may be mistaken for nodular melanoma.

Basosquamous carcinoma

Basosquamous carcinoma is a tumour that has histologic features of both BCC and SCC. These tumours may behave biologically more like a SCC than a BCC, ie have more aggressive behaviour with a greater likelihood of recurring after treatment and potential for metastasis. The incidence of metastasis of this variant of BCC has been estimated to be greater than 5%.

Squamous cell carcinoma

SCC is a cancer of the cells producing keratin. It typically presents as an indurated nodular or crusted tumour that may ulcerate (see Figure 3). SCCs may metastasise and can cause death so need to be identified and treated promptly. The major risk factor for SCC is exposure to ultraviolet (UV) radiation from the sun or sunbeds, especially for fair-skinned people. Immunosuppression is also a significant risk factor. This includes immunosuppression through illness such as HIV infection, blood malignancies, taking immunosuppressant drugs following organ transplant or receiving radiation treatment.

Invasive cutaneous SCC usually arises within a background of sun-damaged skin, most commonly on the bald scalp, face,
neck, extensor forearms, dorsal hands and shin. The colour usually varies from erythematous to flesh-coloured. SCCs are often papulonodular, but can be plaque-like or warty. Some lesions become quite hyperkeratotic with thick crust and other secondary changes including erosions and ulcerations.

The natural history of SCCs also varies, from slowly enlarging to rapidly growing with significant tenderness and pain. Pain is an important symptom as it may be a warning sign of perineural invasion.

Other nonmelanoma skin cancers
There are other much less common NMSC, which can present as fairly innocuous-looking lesions. This emphasises the need to establish a clear histological diagnosis in any rapidly growing nonpigmented skin lesion. An example is dermatofibrosarcoma protuberans (DFSP), a locally aggressive sarcoma of intermediate malignancy that favours young to middle-aged adults. Initially, it presents as a slowly growing, asymptomatic, skin-coloured, indurated plaque. This can resemble a keloid scar. These often occur on the trunk but are locally extremely infiltrative and at high risk of local recurrence. These tumours need radical wide local surgery with or without Mohs micrographic surgery (MMS; see below) to ensure complete excision. Missed or delayed diagnosis causes significant patient morbidity.

Merkel cell carcinoma (MCC) is a rare cutaneous neuroendocrine carcinoma with aggressive clinical behaviour. The tumour favours the head and neck region, followed by the extremities and the buttocks. It usually presents as a pink-red to violaceous, firm, dome-shaped, solitary nodule that has grown rapidly. Surgery is the primary approach. However, owing to the aggressive nature of this tumour, adjuvant chemotherapy and radiation therapy are often administered simultaneously.

Risk factors
The most significant factor in the development of NMSC is exposure to UV light. Intermittent and childhood sun exposure seems to increase the risk of BCC while SCC appears more related to chronic UV exposure. The use of tanning devices significantly increases the risk of NMSC. The risk is greater for SCC than BCC.

Other common factors include having fair skin, red hair, blue eyes and being immunosuppressed. Immunosuppressed patients with skin cancer comprise mainly organ transplant patients and those with chronic haematological malignancies. Patients on biological therapies are an emerging ‘at-risk’ group.

Immunosuppressed patients frequently develop multiple skin cancers, which are often aggressive in nature and at greater risk of metastasis. The incidence of SCC is increased 65- to 250-fold and that of BCC 10-fold. The length of immunosuppression is important, with incidence rates for BCC being 7% after one year and 45% after 11 years. Following a primary SCC, the risk of developing a second NMSC within five years is 66%.

There are genetic mutations, which although rare, can be an important factor in the development of NMSC. In basal cell naevus (Gorlin syndrome), patients develop multiple BCCs. The recent discovery of the mutation of the gene PTCH1 on chromo-

Figure 2. Superficial basal cell carcinoma (BCC) on the back previously treated with cryotherapy

some 9q22, which underlies this rare genetic disorder, has furthered our understanding of the genetics underpinning BCC.

Diagnosis, evaluation and risk stratification
Diagnosis of NMSC is usually clinical with subsequent histological confirmation following excision. The optimal outcome is to ensure a definitive single treatment with a good cosmetic result. Failure to diagnose NMSC early and/or inadequate treatment can result in tumours that destroy important anatomical structures (such as the nose, eye, ear and lip). These can potentially become challenging tumours to treat, often requiring disfiguring surgery, or worse, becoming inoperable. Dermoscopy has been used as an aid for earlier diagnosis of BCC in primary care.

Careful examination of the tumour is important. The main factors to establish are the size, location and whether or not the tumour is recurrent or connects to underlying structures such as muscle, cartilage or bone. The borders should be classified as well or poorly defined and evidence of prior surgery or treatment looked for. These factors significantly affect the management options. If an SCC is suspected, the lymph nodes should be examined. A full examination of the patient’s skin also often reveals other skin cancers.

Histological examination of NMSC is very important. It confirms the clinical diagnosis, identifies the histopathological type of BCC or SCC, and the degree of differentiation of SCC. Histopathological assessment of tumour depth, presence of ulceration, and perineural or vascular involvement are important. All this information combined is used to stratify the tumours into high- and low-risk lesions. High-risk tumours (see Table 1) have greater risk of recurrence and require more aggressive treatment, and so should be identified before treatment commences.
Referral pathways
The importance of multidisciplinary working relationships in the management of high-risk NMSC is important. High-risk NMSC should be referred to secondary care and managed by a skin cancer multidisciplinary team (MDT). Regional cancer networks should establish two levels of MDTs: a local skin MDT and then a regional specialist skin cancer MDT to which more complicated NMSC should be referred. It is recognised that local and specialist MDT referral pathways vary from region to region.

Management options
There is a range of management options for NMSC. High-quality evidence-based studies with long-term follow-up data are found infrequently for NMSC. Choice of treatment in NMSC is dependent on the risk stratification of the tumour, patient preference or suitability, and availability of local services. Treatment may include:

- Surgical excision with defined margins
- MMS
- Radiotherapy
- Curettage and cautery/electrocoagulation
- Cryotherapy/cryosurgery
- Photodynamic therapy (PDT)
- Topical treatment (for example, imiquimod).

For treatments where tissue is not obtained for histological confirmation, such as radiotherapy and PDT, it is expected that the histological diagnosis will have been confirmed before treatment.

Standard excision with predetermined margins
For the majority of BCCs, standard excision with a predetermined margin is the recommended treatment of choice.\(^\text{19}\) Excision of small (<20mm) well-defined BCC with a 3mm peripheral surgical margin will clear the tumour in 85% of cases. A 4–5mm peripheral margin will increase the peripheral clearance rate to approximately 95%.\(^\text{20}\) UK guidelines suggest a 4–5mm excision margin of BCC less than 2cm diameter and of non-morphoeic subtype.\(^\text{21}\)

For SCC, surgical excision with a predetermined margin is the recommended treatment for the majority of SCC. For clinically well-defined low-risk tumours, a margin of 4mm will achieve histological clearance in over 95% of cases.\(^\text{22}\) In high-risk SCC, at least a 6mm margin is recommended. Tumours over 2cm diameter required a 6mm excision margin to provide greater than 95% complete histological cure.\(^\text{23}\)

A recent national audit of practice in the UK of excisions of BCC and SCC found that lateral and deep margins were clear in 98.3% and 99.2% of BCC cases respectively, and in 98.4% and 97.1% of SCC cases respectively.\(^\text{24}\)

Mohs micrographic surgery
MMS was first developed by Frederic Mohs. This is the ‘gold standard’ and optimal treatment for high-risk BCC and SCC. It offers superior excision rates and better cosmetic outcomes as healthy skin removal is kept to a minimum. MMS has been shown to have a greater cure rate than any other treatment modality. A meta-analysis of all published literature on the treatment of BCC and SCC reports MMS to provide a five-year cure rate of 99% for previously untreated BCC and 97% for SCC.\(^\text{23,25}\)

Table 1. Features of high-risk basal cell carcinoma (BCC) and squamous cell carcinoma (SCC)
MMS is a precise technique that combines staged resection with comprehensive histological examination of the whole specimen. During the procedure, the skin cancer is removed in thin layers with a small margin of healthy skin surrounding it. Each layer is immediately checked under the microscope by either the surgeon or a pathologist. Further layers are then taken from any areas where the tumour remains. This is repeated until all of the skin cancer has been fully removed. However, MMS is a limited resource as it is time-consuming, requiring specialised expertise and equipment. Case selection is important, with MMS being mainly reserved for high-risk, recurrent or incompletely excised NMSC or tumours in anatomical sites that require tissue sparing, eg near the eye.

**Radiotherapy**

Radiotherapy is an alternative to surgery for BCCs and SCC of the head and neck region in the following scenarios:

- Elderly or frail patients
- Anatomical sites where radiotherapy is likely to lead to a superior cosmetic or functional outcome, eg nose, ears and lips
- Patients unable or unwilling to undergo surgery

Radiotherapy is not used in younger patients, in previous sites of radiotherapy or in some sites like the lower leg or upper eyelid. Efficacy is lower overall than with MMS or standard excision with predetermined margins. In a meta-analysis, radiotherapy was found to have an overall five-year cure rate of 91.3% for BCC, and 90% for SCC. Adjuvant radiotherapy may be beneficial postoperatively for tumours with perineural invasion or as palliative treatment when complete margin excision is not attainable due to extensive disease. Complications include long-term skin atrophy and necrosis.

**Curettage and cautery**

Curettage and cautery offers an effective treatment of low-risk small (<4mm), well-defined BCC on noncritical sites. In carefully selected cases, curettage and cautery provides a cure rate of 91% at five years. However, with increasing diameter, cure rates are significantly decreased. Curettage and cautery should only be used very cautiously and in specific circumstances in small SCCs. With high-risk SCC, the cure rate is significantly lower, and hence curettage and cautery is not recommended for SCC that may be high risk.

**Cryosurgery**

Cryosurgery is used in low-risk superficial BCC. In this group, a 99% five-year cure rate can be achieved. Cryosurgery is not recommended for SCC as these tumours require histological confirmation and a more definitive therapy such as surgery or radiotherapy. Treatment with cryosurgery can result in hypopigmented scars, and other disadvantages include lack of histological confirmation. Reassessment is also difficult in the event of disease recurrence.

**Photodynamic therapy**

PDT is an effective therapy for sBCC or low-risk nodular BCC of less than 2mm thickness. PDT involves the topical application of 5-aminolevulinic acid (ALA) or methyl aminolevulinic (MAL). Following preferential uptake of the drug into the tumour cells, conversion to protoporphyrin IX (PpIX) occurs. The BCC is then illuminated with 410nm blue or 630nm red light, which activates PpIX and produces a cytotoxic reaction leading to tumour destruction.

Similar efficacy at three months was reported for MAL-PDT and surgical excision in the management of superficial BCC in a large randomised multicentre open study (92.2% clinical lesion response with MAL-PDT vs 99.2% in the surgical group). Higher recurrence rates were observed following PDT, but the cosmetic outcome was superior.

PDT is an established treatment for superficial BCC. In nodular BCC, there is variation in outcome and it is not indicated for the more aggressive basisquamous, morpheic or infiltrating subtypes of BCC or for SCC.

**Imiquimod**

Imiquimod is a topical immunomodulator. It may be a useful treatment for smaller, lower risk BCCs and for patients who

<table>
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<tr>
<th>Criteria for referral of basal cell carcinoma (BCC) to a low-risk BCC service</th>
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<tr>
<td>Patients unable or unwilling to undergo surgery</td>
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<tr>
<td>If the lesion is not located:</td>
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<tr>
<td>• over important underlying anatomical structures (for example, major vessels or nerves)</td>
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<td>• in an area where primary surgical closure may be difficult (for example, digits or front of shin)</td>
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<tr>
<td>• in an area where difficult excision may lead to a poor cosmetic result</td>
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<tr>
<td>• at another highly visible anatomical site (for example, anterior chest or shoulders)</td>
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<td>• where a good cosmetic result is important to the patient</td>
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**Table 2. Criteria for referral of basal cell carcinoma (BCC) to a low-risk BCC service**

The patient is not:

- aged 24 years or younger (that is, a child or young adult)
- immunosuppressed or has Gorlin syndrome

The lesion is:

- is located below the clavicle (that is, not on the head or neck)
- is less than 1cm in diameter with clearly defined margins
- is not a recurrent BCC following incomplete excision
- is not a persistent BCC that has been incompletely excised according to histology
- is not morphoeic, infiltrative or basosquamous in appearance

There is no diagnostic uncertainty that the lesion is a primary nodular low-risk BCC and it meets the following criteria.
**Nonmelanoma skin cancer**

**Squamous cell carcinoma**

- Consider a suspected cancer pathway referral (for an appointment within two weeks) for people with a skin lesion that raises the suspicion of squamous cell carcinoma

**Basal cell carcinoma**

- Consider routine referral for people if they have a skin lesion that raises the suspicion of a basal cell carcinoma
- Only consider a suspected cancer pathway referral (for an appointment within two weeks) for people with a skin lesion that raises the suspicion of a basal cell carcinoma if there is particular concern that a delay may have a significant impact, because of factors such as lesion site or size
- Follow the NICE guidance on **Improving Outcomes for People with Skin Tumours Including Melanoma**: the management of low-risk basal cell carcinomas in the community (2010 update) for advice on who should excise suspected basal cell carcinomas

**Table 3.** NICE guidance on squamous cell carcinoma and basal cell carcinoma. From: NICE. Suspected Cancer: Recognition and Referral. NG12. June 2015

would prefer not to have surgery. In a randomised trial comparing treatment with 5% imiquimod with surgical excision in patients with nodular and superficial BCC, three years after starting treatment, 83.6% of patients who had used imiquimod were treated successfully. This compared with 98.4% who received surgery. There were similar cosmetic outcomes. The main side-effects of the treatment are erythema, crusting, pain, flu-like symptoms and ulceration, which can be severe. Topical imiquimod is not recommended for high-risk BCC or SCC as recurrence rates are too high.

**Topical 5-fluorouracil**

5-fluorouracil is a pyrimidine antimetabolite that inhibits DNA synthesis. Topical treatment has been reported for sBCC. A small study of 17 sBCC showed a 90% histological cure rate at 16 weeks. However, the strength of evidence is lacking and topical 5-fluorouracil is not recommended for first-line treatment of sBCC.

**Management of immunosuppressed patients**

Organ transplant recipients and other patients on long-term immunosuppression who develop NMSC have a higher risk of tumour recurrence. Patients developing multiple SCC may benefit from the introduction of low-dose acitretin to reduce the number of new tumours. If possible, immunosuppressive agents should be maintained at the lowest effective doses.

**Prognosis**

Patients with BCC are at 10 times higher risk of developing a further BCC compared with the general population. Despite this increased risk, no long-term follow-up is required for BCC once the primary tumour has been cured. In the case of SCC, recurrences usually occur within five years. Recommendations vary but for high-risk SCC, patients should be followed up for at least two years and up to five years.

**Conclusion**

BCC and SCC, collectively termed NMSCs, are common and the incidence is increasing. The main risk factor is exposure to sunlight. Evaluation includes skin examination, biopsy and stratification of tumours into high and low risk. This guides appropriate treatment based on risk of recurrence, patient preference or suitability, and availability of local services.

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4. Data were provided by the Office for National Statistics on request, June 2016. Similar data can be found here: http://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/cancerregistrationstatisticsengland/previousReleases
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**Declarations of interest**

None to declare.

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