BJD
British Journal of Dermatology

British Association of Dermatologists guidelines for the management of adults with basal cell carcinoma 2021*

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Accepted for publication

26 May 2021

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Funding sources

None.

Conflicts of interest

C.A.H. has received honoraria as an advisory board member and speaker for Roche, LEO Pharma and Novartis (specific) and for Sanofi, Merck (nonspecific); and has acted as a clinical trial investigator for PellePharm Inc. (specific) and Novartis, LEO Pharma and Meda (nonspecific). P.B. was employed within the healthcare industry (2003–2013; specific). P.G.B. is Deputy Chair of the TVCN Skin Cancer TSSG (specific). K.F. has received honoraria as an advisory board member and speaker for Roche (specific) and sponsorship to attend a meeting from Roche (specific). G.G. has received honoraria as an advisory board member and speaker for Almirall, LEO Pharma and Meda (specific) and from Novartis (nonspecific); and research support from Biofrontera (specific) and LEO Pharma and Meda (nonspecific). S.H. has received honoraria as an advisory board member and speaker from AbbVie and Janssen (nonspecific). J.T.L. has received honoraria as an advisory board member and speaker from LEO Pharma, Meda, Novartis and Roche (specific). E.M. has received sponsorship to attend a meeting from LEO Pharma (specific). C.N. is an investor in a private GP web-based company (nonspecific). E.V.P. has received education sponsorship to attend a dermatology course from LEO Pharma (specific). D.N.S. is a lead on a skin cancer dataset (specific). All other authors declare they have no conflicts of interest.

Produced in 1999 by the British Association of Dermatologists.

*Plain language summary available online

Reviewed and updated 2008, 2021.

DOI 10.1111/bjd.20524

Linked Comment: M.D. Moncrieff and J.P. Nobes. Br J Dermatol 2021; **185**:877.

This is an updated guideline prepared for the British Association of Dermatologists (BAD) Clinical Standards Unit, which includes the Therapy & Guidelines (T&G) subcommittee. Members of the Clinical Standards Unit who have been involved are N.J. Levell (Chairman T&G), B. McDonald (Assistant Honorary Secretary), F.S. Worsnop, P. Rakvit, S.L. Chua, P. Laws, A. Bardhan, L.S. Exton (BAD Guideline Research Fellow), M. Hashme (BAD Information Scientist), M.C. Ezejimofor (BAD Guideline Research Fellow) and M.F. Mohd Mustapa (BAD Clinical Standards Manager).

1. Purpose and scope

The overall objective of the guideline is to provide up-to-date, evidence-based recommendations for the management of basal cell carcinoma (BCC). The document aims to:

- Offer an appraisal of all relevant literature up to 24 January 2020, focusing on any key developments.
- Address important, practical clinical questions relating to the primary guideline objective.
- Provide guideline recommendations and, if appropriate, research recommendations.

The guideline is presented as a detailed review with highlighted recommendations for practical use in primary care [all general practitioners (GPs)], intermediary care [accredited GPs, currently known as a GPs with extended role (GPwERs)] and secondary care (see section 3.0), in addition to an updated patient information leaflet (available on the BAD website, www.skinhealthinfo.org.uk/a-z-conditions-treatments).

1.1. Key exclusions

BCC involving the eyelid has been excluded from this guideline (see section 6.3).

2. Methodology

This set of guidelines has been developed using the BAD's recommended methodology[1] (Appendix J; see Supporting Information) with reference to the AGREE II instrument[2] and GRADE.[3] Recommendations were developed for implementation in the UK National Health Service (NHS).

The Guideline Development Group (GDG) consists of 10 consultant dermatologists (representing England, Northern Ireland, Scotland and Wales; three of whom are also Mohs surgeons), a consultant plastic surgeon, a consultant oral and maxillofacial surgeon, a clinical oncologist, a pathologist, two primary care physicians, a clinical nurse specialist, two patient representatives and a technical team (consisting of an information scientist, two guideline research fellows and a project manager providing methodological and technical support). The GDG established several clinical questions pertinent to the scope of the guideline and a set of outcome measures of importance to patients, ranked according to the GRADE methodology (section 2.1 and Appendix A; see Supporting Information).

A systematic literature search of the PubMed, MEDLINE, Embase and Cochrane databases was conducted to identify key articles on BCC published from 1 January 2007 to 24 January 2020 (publications already included in the 2008 guideline[4] were evaluated for inclusion). Search terms and strategies can be found in Appendix K (see Supporting Information). Additional references relevant to the topic were also extracted from citations in the reviewed literature, and, where identified, relevant articles published after May 2017 were included. Evidence from the included studies was graded according to the GRADE system (high, moderate, low, or very low certainty). Recommendations were based on evidence drawn from systematic reviews of the literature pertaining to the clinical questions identified. The Supporting Information includes the summary of findings with forest plots (Appendices B and C; see Supporting Information), tables Linking the Evidence To the Recommendations (LETR) (Appendix D; see Supporting Information), GRADE evidence profiles indicating the certainty of the evidence (Appendix E; see Supporting Information), a summary of included comparative studies (Appendix F; see Supporting Information), narrative findings for noncomparative studies (Appendix G; see Supporting Information), a PRISMA flow diagram (Appendix H; see Supporting Information) and lists of studies excluded from quantitative analyses with reasons for exclusion (Appendix I; see Supporting Information). The strength of recommendation is expressed by the wording and symbols shown in Table 1.

2.1. Low-risk and high-risk basal cell carcinoma criteria

Following review of the literature the GDG agreed to adopt the Royal College of Pathologists (RCPath) dataset.[5] The dataset defines pathological low-risk and high-risk BCC based on increased risk for local recurrence and very occasionally metastasis, especially if there is perineural invasion in any type of BCC and/or lymphovascular invasion in basosquamous carcinoma. Clinical factors that confer low-risk vs. high-risk BCC are defined as per the National Institute for Health and Care Excellence (NICE), based on reducing the risks of incomplete excision, recurrence following surgery, and damaging important, proximate anatomical features, to achieve good cosmetic results and reduce postsurgical complications.[6] NICE also considered the skills and training of the surgical operator. The National Comprehensive Cancer Network (NCCN) guidelines[7] gave more precise clinical criteria for clinical low-risk and high-risk BCC. As the Union for International Cancer Control 8th edition (UICC8)[8] version of TNM8 (tumour–nodes–metastasis) has been endorsed for use in the UK, and as NCCN uses the American Joint Committee on Cancer 8th edition cancer staging manual (AJCC8),[9] the NCCN table on low-risk and high-risk BCC criteria has been adapted here to equate to the UICC8 and RCPath dataset.

The GDG's adopted definition of criteria for low-risk and high-risk BCC is provided in Table 2.

The GDG identified a paper that provided a definition for advanced BCC,[10] but it was dependent on the AJCC7 risk criteria. The GDG adopted the definition with some adaptation to be used in this guideline, as follows:

> 'An advanced BCC is a BCC that is either (i) metastatic (mBCC) or (ii) locally advanced (laBCC) with one or more high-risk factors, in which current treatment modalities are considered potentially contraindicated by tumour or patient factors'.

Clinical tumour factors that may contribute individually or in combination to a BCC being regarded as locally advanced include:

- Tumour size and location, and cosmetic and functional consequences of treatment (e.g. 'giant' BCC, which is > 5 cm and/or would require extensive surgery such as amputation; and H-zone tumours; Figure 1).
- Large numbers of coexisting tumours.
- Tumour subtype (e.g. infiltrative tumours with poorly defined margins).
- Likelihood of successful treatment compromised by previous treatment (e.g. multiple recurrences of BCC after surgery or previous radiotherapy).

Patient-driven factors that may contribute individually or in combination to a BCC being regarded as locally advanced include:

- Patient performance status (e.g. compromised due to age or frailty).
- Presence of patient comorbidities potentially interfering with surgery (e.g. unsuitability for general anaesthetic).
- Presence of patient factors potentially interfering with radiotherapy (e.g. contraindicated in Gorlin syndrome and relatively contraindicated in younger patients).
- Patient opinions and beliefs regarding treatment and/or their impact on quality of life [e.g. unwilling or reluctant to accept consequences of surgery such as poor cosmetic outcome or adverse effects (AEs) of radiotherapy].

2.2. Clinical questions and outcomes

The GDG established a number of clinical questions pertinent to the scope of the guideline (Appendix A; see Supporting Information). The GDG also established a set of outcome measures of importance to patients for each clinical question; these outcomes

Table 1 Strength of recommendation ratings

Strength	Wording	Symbol	Definition
Strong recommendation *for* the use of an intervention	'Offer' (or similar, e.g. 'use', 'provide', 'take', 'investigate' etc.)	↑↑	Benefits of the intervention outweigh the risks; most patients would choose the intervention while only a small proportion would not; for clinicians, most of their patients would receive the intervention; for policymakers, it would be a useful performance indicator
Weak recommendation *for* the use of an intervention	'Consider'	↑	Risks and benefits of the intervention are finely balanced; many patients would choose the intervention, but many would not; clinicians would need to consider the pros and cons for the patient in the context of the evidence; for policymakers it would be a poor performance indicator where variability in practice is expected
No recommendation		Θ	Insufficient evidence to support any recommendation
Strong recommendation *against* the use of an intervention	'Do not offer'	↓↓	Risks of the intervention outweigh the benefits; most patients would *not* choose the intervention while only a small proportion would; for clinicians, most of their patients would *not* receive the intervention

Table 2 Criteria for low-risk and high-risk basal cell carcinoma (BCC)

	Low risk	High risk[a]
Clinical criteria		
Location and size	Area L[b] ≤ 20 mm (maximum clinical diameter) Area M[c] ≤ 10 mm (maximum clinical diameter)	Area L[b] > 20 mm (maximum clinical diameter) Area M[c] > 10 mm (maximum clinical diameter) Area H[d]
Borders	Well defined	Poorly defined
Primary vs. recurrent	Primary	Recurrent
Immunosuppression	No	Yes
Site of prior radiotherapy	No	Yes
Pathological criteria		
BCC and stage		
Growth pattern	Nodular or superficial	Infiltrative (infiltrating, morphoeic, micronodular)
Differentiation: basosquamous	Absent	Present (with or without lymphovascular invasion)
Level of invasion	Dermis, subcutaneous fat	Beyond subcutaneous fat
Depth (thickness)	≤ 6 mm	> 6 mm
Perineural invasion[e]	Absent	Present
Pathological TNM stage	pT1 ≤ 20 mm (maximum diameter)	pT2 > 20 mm but ≤ 40 mm (maximum diameter) pT3 > 40 mm (maximum diameter), or upstaged[f] pT1 or pT2, or minor bone invasion pT4 major bone invasion
Margins		
Histological margins	Not involved (≥ 1 mm)	Involved (0 mm) or histologically close (< 1 mm)

TNM, Tumour–Nodes–Metastasis. [a]One or more criteria equals high risk, unless stated differently in the summary of the recommendations, or in an explanatory note. [b]Area L = trunk and extremities ***but excluding*** hands, nail units, genitals, pretibia, ankles and feet. [c]Area M (see Figure 1) = cheeks, forehead, scalp, neck and pretibia. [d]Area H (see Figure 1) = 'mask areas' of face [central face, eyebrows, periorbital, nose, lips (cutaneous and vermilion), chin, mandible, preauricular, postauricular, temple, ears]; genital areas; hands, nail units, ankles and feet, but ***excluding the eyelid***. For tumours < 6 mm in size without other high-risk features, standard surgical excision may be considered if a ≥ 4 mm clinical surgical margin can be obtained without significant anatomical or functional distortions. [e]A named nerve or a diameter ≥ 0·1 mm or beyond the dermis. [f]T1 and T2 can be upstaged to T3 by the presence of one or more high-risk clinical or pathological factors comprising specifically defined perineural invasion or deep invasion representing either a tumour thickness or depth > 6 mm and/or invasion beyond or further than the subcutaneous fat.

were ranked by the patient representatives according to the GRADE methodology from 1 to 9.[3] Outcomes ranked 7, 8 or 9 were critical for decision making; those ranked 4, 5 or 6 were important but not critical for decision making. Data on these outcome measures were extracted from the included studies (Appendices B, C, E, F and G; see Supporting Information). The outcomes are given along with their ranking score.

Review question 1: treatment for high-risk BCC

In people with high-risk BCC, what are the clinical effectiveness and cost-effectiveness of surgical (standard and Mohs) and nonsurgical techniques [topical therapies, photodynamic therapy (PDT), radiotherapy and biologic therapies] compared with each other or with no treatment (observation)?

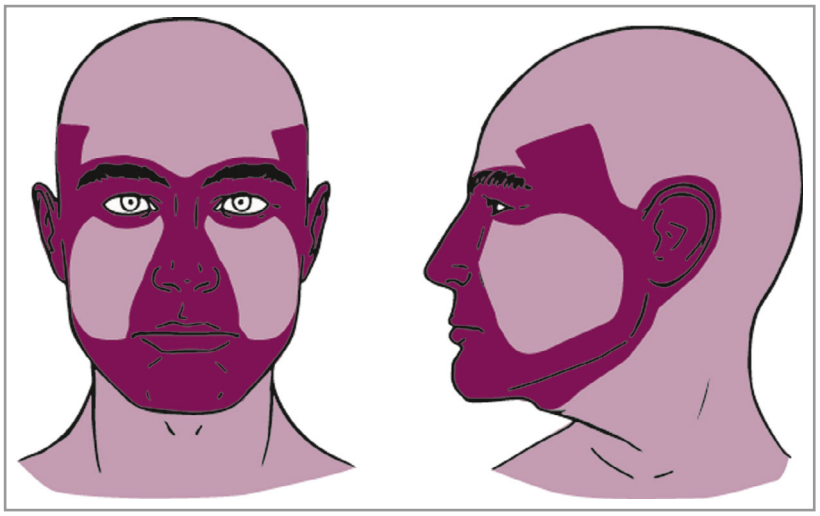

Figure 1 Areas H (darker shade) and M (lighter shade) on the head and neck

- Complete response or clearance (9).
- Recurrence rate (above clavicle) (9).
- Treatment-related serious AEs (nonsurgical) or complications (surgery) (8).
- Functional outcome (physical or social functioning) (8).
- Cosmesis (7).
- Convenience of treatment and patient choice (7).
- Partial (> 50%) response or clearance (6).

Review question 2: treatment for low-risk BCC

In people with low-risk BCC, what are the clinical effectiveness and cost-effectiveness of surgical (standard and Mohs) and nonsurgical techniques (topical therapies, PDT, radiotherapy and biologic therapies) compared with each other or with no treatment (observation)?

- Complete response or clearance (9).
- Convenience of treatment (9).
- Treatment-related serious AEs (nonsurgical) or complications (surgery) (8).
- Cosmesis (7).
- Recurrence rate (below clavicle) (6).
- Partial (> 50%) response or clearance (6).

Review question 3: surgical margins

In people with BCC who undergo standard surgical excision, what surgical margins should be used?

- Recurrence rate (9).
- Incomplete excision (7).

Review question 4: follow-up

In people with high-risk BCC, what is the appropriate follow-up period following treatment, including surgical (standard and Mohs) and nonsurgical techniques (topical therapies, PDT, radiotherapy and biologic therapies) or no treatment?

- Recurrence rate (9).

Review question 5: clinical settings

In people with a high-risk BCC, would referral to the 'next care level' [primary to secondary or secondary to multidisciplinary (MDT)] lead to a decreased chance of having to undergo re-excision?

- Recurrence rate (9).
- Incomplete excision (9).

3. Summary of recommendations

The majority of the recommendations and ratings were agreed upon unanimously by the core members of the GDG and patient representatives following extensive discussions. Where the GDG disagreed on specific issues, votes were cast on all options put forward, and the simple-majority results were featured as the final decision. (For further information on the wording used for recommendations and strength of recommendation ratings, see Table 1.) The GDG is aware of the lack of high-certainty evidence for some recommendations, therefore, strong recommendations with an asterisk (*) are based on available evidence, as well as informal consensus and specialist experience amongst GDG members. Good practice point (GPP) recommendations are derived from informal consensus among GDG members. In general, patient choice should be factored into the decision-making process in applying all the recommendations listed below.

For the relevant recommendations listed below, see †Table 2 for the criteria for low-risk and high-risk BCC, ¶section 2.1 for the definition of advanced BCC, and ¥Table 3 for levels of community skin cancer services. Where §a patient declines treatment this could also be the patient's representative with power of attorney.

General

R1 ↑↑ Offer* verbal and written information about BCC to all adults with BCC, including the nature and prognosis of BCC, available treatment options and the ongoing need for sun protection and self-surveillance of their skin as part of prevention or early detection of future skin tumours.

Referral from primary care

R2 ↑↑ Refer* to a local skin multidisciplinary team (LSMDT) or a specialized skin cancer multidisciplinary team

(SSMDT) member all adults with high-risk† BCC, and all adults with low-risk† BCC in the absence of an accredited¥ General Practitioner with Enhanced Role (GPwER) or if the primary care facility is not suitable for surgery. See Table 3 for levels of community skin cancer services.

Surgical treatment

R3 ↑↑ Offer* standard surgical excision as a first-line treatment option to adults with low-risk† BCC.

R4 ↑↑ Offer* standard surgical excision with **immediate** reconstruction as a first-line treatment option to adults with **primary** BCC with a high-risk factor,† if the BCC has **well-defined** clinical margins under bright lighting and magnification or dermoscopy.

R5 ↑↑ Offer* standard surgical excision with **delayed** definitive reconstruction, or Mohs micrographic surgery, as the first-line treatment option to adults with high-risk† BCC within a high-risk anatomical site if the BCC has **poorly defined** clinical margins under bright lighting and magnification or dermoscopy.

R6 ↑↑ Excise* low-risk† BCC using a 4 mm peripheral clinical surgical margin.

R7 ↑↑ Excise* primary BCC with a high-risk factor† using at least a 5 mm peripheral clinical surgical margin (see also **R4** and **R5**).

R8 ↑↑ Excise* BCC by ensuring adequate excision at the deep margin to a clear plane, including a fat layer where present, and other deeper structures if needed.

R9 ↑ Consider Mohs micrographic surgery in adults with **primary** BCC with at least one high-risk factor.†

R10 ↑↑ Offer* Mohs micrographic surgery as a first-line treatment option to adults with recurrent BCC with at least one other high-risk factor,† especially if the tumour is at a high-risk site.

R11 ↑ Following discussion at an MDT, consider standard surgical excision with at least a 5 mm margin and delayed definitive reconstruction as a treatment option to adults with **recurrent** BCC with at least one other high-risk factor.†

R12 ↑↑ Offer* standard surgical excision or radiotherapy as a treatment option to adults with **advanced**¶ BCC (see also **R14**).

R13 ↑ Consider Mohs micrographic surgery as a treatment option to adults with **advanced**¶ BCC.

Systemic therapy

R14 ↑↑ Offer* vismodegib, subject to availability, as a treatment option to adults with **advanced**¶ BCC who are unsuitable for Mohs micrographic surgery, standard surgical excision or radiotherapy, including patients with Gorlin syndrome, following discussion at an MDT (see also **R12** and **R13**).

Radiotherapy

R15 ↑↑ Offer* radiotherapy as a treatment option to adults (suggested age ≥ 60 years) with low-risk and high-risk BCC who are unsuitable for or decline§ Mohs micrographic surgery or standard surgical excision and who express a preference for radiotherapy, and in whom the lesion is:

- a nodular BCC
- an infiltrative subtype of BCC, provided a sufficient planning margin is used
- an excised BCC with involved margins

R16 ↓↓ Do not offer* radiotherapy as a treatment option to adults with BCC who are unsuitable for or decline§ Mohs micrographic surgery or standard surgical excision, and in whom the lesion is:

- a **recurrent** BCC following previous radiotherapy
- associated with certain genetic syndromes predisposing to skin cancers, for example Gorlin syndrome or xeroderma pigmentosum

Discuss alternative treatment modalities at an MDT (see **R1**, **R3–5**, **R9–14** and **R18–23**).

R17 ↓↓ Do not routinely offer* radiotherapy as a treatment option to adults with BCC who are unsuitable for or decline§ Mohs micrographic surgery or standard surgical excision, and in whom the lesion is:

- on areas of poor blood supply (e.g. the lower limbs)
- in younger patients in whom the late effects of radiotherapy could be an issue (suggested age < 60 years)
- a BCC invading bone or cartilage

Discuss alternative treatment modalities at an MDT (see **R1**, **R3–5**, **R9–14** and **R18–23**).

Other treatment options

R18 ↑↑ Offer* topical imiquimod, topical 5-fluorouracil, cryosurgery or topical PDT as treatment options to adults with low-risk† BCC who are unsuitable for or decline§ standard surgical excision.

R19 ↓↓ Do not offer* topical imiquimod, topical 5-fluorouracil, cryosurgery, curettage and cautery, or topical PDT as treatment options to adults with high-risk† BCC who are unsuitable for or decline§ Mohs micrographic surgery or standard surgical excision.

R20 ↓↓ Do not offer* topical imiquimod, topical 5-fluorouracil, cryosurgery or topical PDT as a treatment option to adults with **advanced**¶ BCC unless for palliation of symptoms, following discussion at an MDT.

R21 ↑↑ Advise* adults with BCC who decline§ all treatments that the risk of significant progression of the tumour is at least 25% over 2–5 years.

Θ1 There is insufficient evidence to support any recommendation for the following interventions for low-risk (including **recurrent**, low-risk) BCC:†

- Mohs micrographic surgery
- vismodegib

Θ2 There is insufficient evidence to support any recommendation for the following interventions for BCC:

- topical ingenol mebutate gel.
- topical Curaderm-BEC5 cream.
- electrochemotherapy (ECT).
- CO_2 laser.
- pulsed-dye laser.
- combinations of:

Table 3 Levels of community skin cancer services

Group of GPwER	Status	Range of activity[a]
Group 1: GPwER in general dermatology (*nonsurgical*)	A GP who has suitable training and has demonstrated competency in general dermatology	Diagnosis and management of inflammatory skin disease; diagnosis of skin lesions and their *nonsurgical* management, including topical therapy and PDT; and *nonexcisional surgical* procedures, including cryosurgery and curettage and cautery, depending on their training level and availability of treatment, for low-risk BCC and also precancerous lesions, e.g. actinic keratoses and SCC *in situ* (Bowen disease)
Group 2: GPwER in skin lesion management	A GP who has suitable training and has demonstrated competency in skin lesion management	Diagnosis and management of skin lesions, including low-risk BCC [well-defined bordered primary nodular or superficial BCC on area L[b] ≤ 20 mm (maximum clinical diameter) and on area M[c] ≤ 10 mm (maximum clinical diameter)], using both surgical and nonsurgical techniques, relevant to their clinical training. In addition, group 2 and 3 GPwERs are expected to follow those aspects of the NICE recommendations[e] relevant to their agreed scope of practice
Group 3: GPwER in general dermatology and skin lesion management	A GP who has suitable training and has demonstrated competency in general dermatology and skin lesion management	This group combines groups 1 and 2
Model 2 practitioner	A skin surgeon who might be a GP, nurse specialist or secondary care specialist working in the community under the governance of an acute trust	Management of skin lesions discussed with a core LSMDT member and within the practitioner's competencies recognized by the LSMDT

BCC, basal cell carcinoma; GP, general practitioner; GPwER, GP with Enhanced Role; LSMDT, Local Skin Multidisciplinary Team; NICE, National Institute for Health and Care Excellence. [a]No community practitioner should knowingly treat high-risk BCC, especially on areas M[c] or H[d]; recurrent BCC; or BCC with high-risk pathological criteria, except after discussing it with the LSMDT. [b]Area L = trunk and extremities ***but excluding*** hands, nail units, genitals, pretibia, ankles and feet. [c]Area M = cheeks, forehead, scalp, neck and pretibia. [d]Area H = "mask areas" of face (central face, eyebrows, periorbital, nose, lips (cutaneous and vermilion), chin, mandible, preauricular, postauricular, temple, ears); genital areas; hands, nail units, ankles and feet, ***but excluding the eyelid***. [e]NICE[6] recommends that, for ***all*** groups of GPs managing BCC in the community, the patient is not aged 24 years or younger, is not immunosuppressed and does not have Gorlin syndrome, and also that the lesion (i) is located below the clavicle (area L), (ii) is < 1 cm in diameter with clearly defined margins, (iii) is not a recurrent BCC following incomplete excision, (iv) is not a persistent BCC that has been incompletely excised according to histology, (v) is not morphoeic, infiltrative or basosquamous in appearance and (vi) is not located (A) over important underlying anatomical structures (e.g. major vessels or nerves), (B) in an area where primary surgical closure may be difficult (e.g. digits or front of shin), (C) in an area where difficult excision may lead to a poor cosmetic result, or (D) at a highly visible anatomical site (e.g. anterior chest or shoulders) where a good cosmetic result is important to the patient. If the lesion is thought to be a superficial BCC the GP should ensure that the patient is offered the full range of medical treatments (including topical therapy and PDT) and *nonexcisional surgical* procedures, including cryosurgery and curettage and cautery, which may require referral to a member of the LSMDT.

- Topical diclofenac + calcitriol.
- Topical imiquimod + Mohs micrographic surgery.
- Intralesional interferon-α + standard surgical excision.
- Topical PDT + Mohs micrographic surgery.
- Laser therapy + topical PDT.

Θ3 There is insufficient evidence to recommend 'no treatment' as an option for adults with:

- **recurrent** BCC with at least one other high-risk factor.
- **advanced** BCC who are not suitable for or decline[§] Mohs micrographic surgery or standard surgical excision.

Management following primary treatment

R22 ↑↑ Following discussion at an MDT, offer* further standard surgical re-excision to adults with excised high-risk[†] BCC with involved histological margin unless there is a contraindication (see also **R4**, **R5**, **R7–21**, **Θ1**, **Θ2** and **Θ3**).

R23 GPP Refer all adults with excised high-risk[†] BCC with a close histological margin (< 1 mm) for MDT discussion of management options. These may include surgical re-excision, Mohs micrographic surgery, radiotherapy or monitoring. Patient choice should especially be factored into the decision-making process in such a situation.

R24 ↓↓ Do not routinely offer* follow-up to patients with adequately treated isolated BCC, unless for a postoperative review (see also **R25** and **R26**).

R25 GPP Offer, if possible, a postoperative review of adults with adequately treated BCC by an appropriate healthcare professional, in either secondary or primary care.

R26 GPP Offer, if possible, at least yearly follow-up to adults with a history of multiple BCCs who are likely to develop further tumours or recurrence within 12 months.

Summary of future research recommendations

The following list outlines future research recommendations (FRRs).

FRR1 Randomized controlled trials (RCTs) comparing standard surgical re-excision of high-risk BCC excised with close (< 1 mm) or involved histological margin vs. Mohs micrographic surgery, radiotherapy or no treatment. Primary outcomes should include recurrence rate over at least 5 years.

FRR2 RCTs directly comparing various treatment modalities with primary outcomes to include UK health economic assessment (including treatment of recurrences) and patient-reported outcome measures.

FRR3 RCTs comparing standard surgical excision vs. Mohs micrographic surgery for high-risk BCC, with longer follow-up periods of *at least* 5 years.

4. Algorithm

The recommendations, discussions in the LETR sections (Appendix D; see Supporting Information) and consensus specialist experience were used to produce management pathways for adults with BCC – see Figure 2 and Tables 4–8.

5. Background

5.1. Definition

BCC is the most common keratinocyte cancer (KC)/non-melanoma skin cancer (NMSC).[11–15] It is a slow-growing, locally invasive malignancy that very rarely metastasizes.[7,10,14] Usually it develops on sun-exposed areas such as the head and neck,[13,14] although potentially any cutaneous site can be affected. Clinically and pathologically, BCC is heterogeneous. The most common subtype is nodular BCC (> 60%),[10] and other variants include superficial, infiltrative (morphoeic, sclerosing, micronodular), keratotic and pigmented are also described, with frequent histological overlap between types.[11] The basosquamous variant is the most aggressive type. It has a tendency for lymphovascular or perineural invasion, and can rarely metastasize.[7,11] BCC usually develops as a sporadic tumour but rarely it can develop in chronic scars[16] or be part of a genodermatosis, for example Gorlin syndrome, xeroderma pigmentosum, Bazex–Dupré–Christol syndrome and Rombo syndrome.[10,11,13]

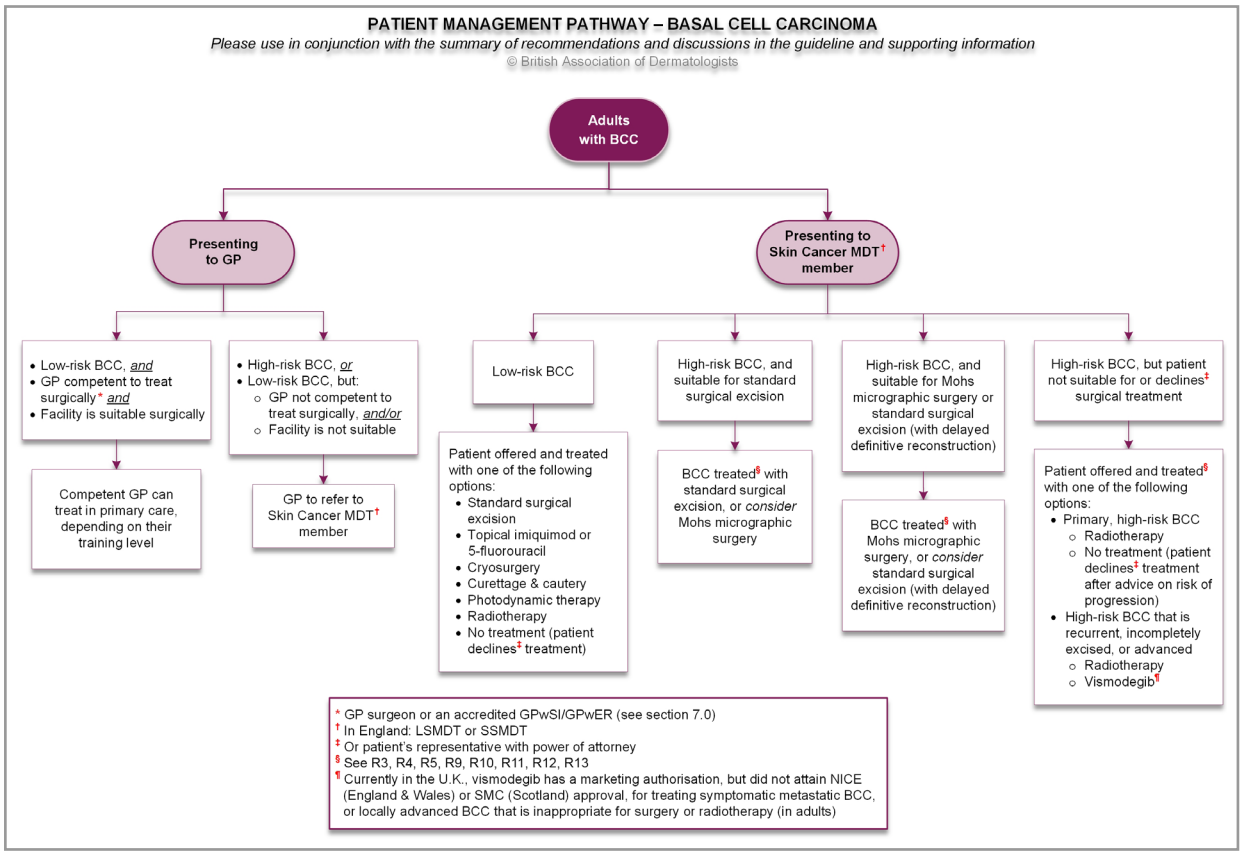

Figure 2 Basal cell carcinoma management pathway in primary, secondary and tertiary care. BCC, basal cell carcinoma; GP, general practitioner; GPwER, GP with Extended Role; GPwSI, GP with Special Interest; LSMDT, Local Skin MDT; MDT, Multidisciplinary Team; NICE, National Institute for Health and Care Excellence; SMC, Scottish Medicines Consortium; SSMDT, Specialist Skin Cancer MDT

Table 4 Primary basal cell carcinoma (BCC) *suitable for surgery*: influence of tumour risk on the selection of treatment

	Strength of recommendation	
Treatment	Low-risk BCC	High-risk BCC
Excisional surgery	↑↑	↑↑[a]
Mohs micrographic surgery	Θ	↑↑

[a] Please refer to summary of recommendations R4, R5, R7 and R8 for details.

Table 5 Primary basal cell carcinoma (BCC) *not suitable for or patient declines surgery*: influence of tumour risk on the selection of treatment

	Strength of recommendation	
Treatment	Low-risk BCC	High risk-BCC
Radiotherapy	↑↑[a]	↑↑[a]
Vismodegib	Θ	↑[b]
Topical agents (imiquimod or 5-fluorouracil)	↑↑	↓↓
Cryosurgery	↑↑	↓↓
Curettage and cautery without subsequent surgery	↑↑	↓↓
Photodynamic therapy	↑↑	↓↓
No treatment (patient declines treatment)[c]	↑	Θ[d]

[a] Please refer to summary of recommendations R15–R17 for details. [b] Please refer to summary of recommendations R14 for details. [c] Or patient's representative with power of attorney. [d] Please refer to summary of recommendations R21 for details.

Table 6 Recurrent basal cell carcinoma (BCC) *suitable for surgery*: influence of tumour risk on the selection of treatment

	Strength of recommendation	
Treatment	Low-risk BCC	High-risk BCC
Excisional surgery	↑↑	↑[a]
Mohs micrographic surgery	Θ	↑↑

[a] Please refer to summary of recommendations R4, R5 and R7–R11 for details.

Table 7 Recurrent basal cell carcinoma (BCC) *not suitable for or patient declines surgery*: influence of tumour risk on the selection of treatment

	Strength of recommendation	
Treatment	Low-risk BCC	High-risk BCC
Radiotherapy	↑↑[a]	↑↑[a]
Vismodegib	Θ	↑
Topical agents (imiquimod or 5-fluorouracil)	↑	↓↓
Cryosurgery	↑	↓↓
Curettage and cautery without subsequent surgery	↑	↓↓
Photodynamic therapy	↑	↓↓
No treatment (patient declines treatment)[b]	↑	Θ[c]

[a] Please refer to summary of recommendations R15–R17 for details. [b] Or patient's representative with power of attorney. [c] Please refer to summary of recommendations R21 and Θ3 for details.

Table 8 Advanced basal cell carcinoma (metastatic or locally advanced): strength of recommendation for treatments

Treatment	Strength of recommendation
Excisional surgery	↑↑
Mohs micrographic surgery	↑
Radiotherapy	↑↑
Vismodegib	↑↑
Topical agents (imiquimod or 5-fluorouracil)	↓↓
Cryosurgery	↓↓
Curettage and cautery without subsequent surgery	↓↓
Photodynamic therapy	↓↓
No treatment (patient declines treatment)[a]	Θ[b]

[a] Or patient's representative with power of attorney. [b]Please refer to summary of recommendations R21 and Θ3 for details.

5.2. Incidence and aetiology

The exact incidence of BCC globally is not accurately known because it is not included in cancer registries in most countries.[13–15] However, recent improvements to registry data collection in England have enabled more accurate analysis, which has confirmed a rise in incidence of the first BCC per person per year from 268 565 in 2013 to 410 716 in 2015.[15] Incidence increases with age and BCC is more common in men.[15]

BCC is an epidermal KC. The exact cell of origin is not known, although it is considered to originate from pluripotent cells in the interfollicular epidermis and infundibulum of the hair follicle distributed along the basal layer.[17,18] It is believed to be caused by a combination of genetic predisposition and exposure to ultraviolet radiation, and the risk is increased in the context of immunosuppression, for example organ transplantation,[19] HIV[20] and haematological malignancy.[11,13] The hedgehog intracellular signalling pathway is critical for the regulation of cell growth and differentiation in embryonic development. Development of BCC is associated in most cases with loss of inhibition of hedgehog signalling. This is the result of inactivating mutations in the tumour-suppressor protein patched homologue 1 gene (*PTCH1*) in 90% of sporadic BCC and activating mutations in the smoothened transmembrane protein gene (*SMO*) in 10% of cases, with germline mutations in *PTCH1* and occasionally *PTCH2*, *SMO* and suppressor of fused (*SUFU*) genes in Gorlin syndrome. The importance of this pathway is highlighted by the successful use in advanced BCC of hedgehog pathway inhibitors (e.g. vismodegib).[10,11,14,18]

6. Diagnosis and investigation

6.1. Diagnosis

Dermatologists and other skin cancer specialists can usually diagnose BCC clinically, without the need for biopsy. Diagnostic accuracy is enhanced by good lighting, the skin stretch test[21] and dermoscopy.[22,23] Specialist noninvasive skin imaging tools, including reflectance confocal microscopy and optical coherence tomography, may also help in diagnosis of difficult cases, although these are not widely available.[24–26]

Biopsy is indicated if there is clinical doubt about the diagnosis, for potentially high-risk types (e.g. based on clinical risk factors of size and/or location), if the treatment will be influenced by histological subtype (e.g. infiltrative vs. superficial) and to confirm recurrences after treatment.[7,11,12,14] In most cases, shave or curette biopsy should be sufficient to make a positive diagnosis of BCC.[11] If the histological subtype is in doubt, a deep incisional or excisional biopsy (to include the dermis or fat, if possible) is recommended.[12,14]

If there is clinical suspicion that the tumour is attached to or extends deep into the underlying deep fascia, and/or if there is suspected involvement of muscle, large nerves, blood vessels or bone, then cross-sectional imaging of the area using either computed tomography (CT) scanning or magnetic resonance imaging (MRI) should be considered, and the case should be discussed at an SSMDT meeting prior to treatment.[7,12,14] In the case of involvement of deeper structures of the head and neck area, referral to the head and neck MDT may be considered.[7,12,14]

6.2. Low-risk and high-risk tumours, patient factors and treatment selection

The management of BCC depends on a number of factors including the size, site and histological subtype of the tumour (Table 2), patient comorbidities, previous treatment history and patient preference.[10] It is also important to consider whether the intention of treatment is curative or palliative, where and by whom treatment should be delivered to ensure the best possible outcome (see section 7), and the availability of treatment within the treating healthcare provider's service.

The GDG identified only one publication[27] that addresses the needs and preferences of patients regarding BCC and squamous cell carcinoma (SCC) treatment. This qualitative study found that of particular importance to patients with BCC were to receive relevant information tailored to their specific situation, to be seen by the same physician during treatment and follow-up, to have a full-body skin examination during follow-up, and to participate in shared decision making.

Factors that should be considered in making a joint decision regarding treatment include:

- performance status of the patient
- risk of the particular tumour in causing harm if not treated (e.g. the presence of ulceration, bleeding, rapid growth, and proximity to or involvement of important structures such as the eye and bony orifices)
- presence of comorbidities, including serious, life-limiting conditions
- presence of genodermatoses (e.g. Gorlin syndrome)
- presence of compromised immune status
- regular medications taken by the patient, especially anticoagulants and those that adversely modify wound healing
- risk of morbidity or mortality associated with treatment of the BCC
- the likelihood of treatment success
- whether the patient has an implanted cardiac device

As BCC is a slow-growing, often asymptomatic tumour that rarely metastasizes, in certain circumstances the option of 'no treatment' arises. This may seem an attractive option if the patient has a short life expectancy, but the healthcare provider needs to ensure that the patient fully understands the risks of locally advanced disease.[10,12] A case series of five patients with low-risk BCC demonstrated that they progressed to advanced BCC within 2 years.[28] Retrospective studies of patients who did not have re-excision for incompletely excised BCCs showed recurrence rates of at least 25% over 5 years.[29,30]

6.3. Eyelid

For several editions of TNM, staging of the eyelid has been specifically excluded from staging of BCC of the entire skin. The eyelid has been allocated its own specific and different staging system for the primary tumour and lymph nodes. For many reasons (including clinical, pathological and cancer registration) it is essential that this different system for the eyelid is better recognized and used by clinicians, pathologists and skin cancer MDTs. Regarding its management, a BCC of the eyelid of combined lowest pT1 stage and low-risk histological status still constitutes a high-risk BCC as it is situated in area H. This would mandate management considerations similar to all high-risk BCCs in area H, namely with either Mohs micrographic surgery or standard surgical excision with delayed definitive reconstruction – see R4, R5, R9–21 and Θ3.

6.4. Digital photography

The diagnosis and management of skin disorders can be aided by digital photography for clear documentation, and to monitor treatment response.[31] BCC is no exception to this, where healthcare professionals can utilize it with or without digital dermoscopy photography. Digital photography is also useful in helping patients with regular self-examination of their skin.[32] Total-body digital photography can be available for use in clinic, while patients can use digital applications to store these photographs on their personal devices.[33]

However, some limitations and challenges have been reported, such as the lack of standardization in ensuring the same position, imaging angle and lighting every time, highly expensive devices and equipment, and the time needed to have

the photographs taken.[34] It is envisaged that in the future, advances in technology might make digital photography for skin cancer, including BCC, more efficient and cheaper.[34]

The GDG agrees with the utility of digital photography, where possible, in the management of BCC, and highlights the following:

- No image should be kept without the patient's express consent, and in line with the NHS data protection and information governance requirements.
- As remote consultations (e.g. teledermatology) increasingly become the new norm, even prior to the COVID-19 pandemic, patients should be informed of the risks associated with forwarding of digital images. Information governance and data protection rules do not apply until the images have reached the healthcare provider.[35]
- Images should become part of the patient's lifelong clinical records.
- Images should demonstrate both anatomical location and close-to-detail features (plus dermoscopic detail, if available).
- Where multiple lesions exist, each should be annotated separately.

7. Management

Overview

In most cases of primary BCC, surgery is the recommended treatment modality.[11] 'Surgery' includes those forms of surgical treatment with postoperative margin assessment such as standard surgical excision and Mohs micrographic surgery, and those without postoperative margin assessment, such as curettage and cautery, cryosurgery and laser therapy.[11,12,14] Each surgical technique has its own indications and contraindications (see sections 7.4, 7.5, 7.6 and 7.7). Other treatment modalities such as radiotherapy, topical therapies and PDT may be offered if the patient is not suitable for or declines surgery; selection of each modality depends on the precise clinical scenario. In advanced BCC (mBCC and laBCC), surgery may not be feasible, and alternative options include radiotherapy and hedgehog pathway inhibitors.

7.1. Considerations: the patient

The patient, or the person with the power of attorney for health matters, should be counselled sufficiently on all aspects of the treatment approach being considered and post-treatment care, especially with respect to the possibility of developing a scar. Patients should be informed of methods to improve cosmetic outcome following primary treatment. If psychological need has been identified, a referral should be made to appropriate services and a key worker should be identified to support the patient during this process.

At diagnosis, all patients with BCC should be given tailored advice in the forms of verbal and written information. This should include information regarding the nature, prognosis and treatment options for BCC, predisposing factors (especially sun exposure), advice on photoprotection (with accompanying advice on implications of photoprotection for vitamin D status), risk of recurrence or development of new primary skin cancers, and the importance of early detection of recurrence or new tumours by self-skin examination. All patients should be directed as to how to access clinical assessment rapidly should a suspicious lesion arise.

7.2. Considerations: the clinical practitioner

One important issue in management of BCC in the UK is that not all clinicians involved in providing treatment have the same specific skills. For example, some are competent in treating low-risk BCC in the primary care setting, while others in the secondary care setting have advanced surgical skills either for all anatomical areas affected (L, M, H) or for particular areas only, for example areas L and M (Table 2). Others are clinical or medical oncologists who treat advanced BCC with radiotherapy and/or systemic agents, respectively.

Primary care/community-based practitioners can choose to develop the necessary knowledge and skills to undertake skin cancer diagnosis and treatment. All GPs providing skin cancer treatment should demonstrate the necessary knowledge and skills commensurate with their level of activity. Those currently known as a GPwER are accredited by a team appointed by the Royal College of General Practitioners (RCGP) to meet the skills described in the current NICE guidance 2010[6] and the RCGP framework 2018 (see Table 3).[36]

7.3. Multidisciplinary team

One of the main service provisions for management of skin cancers, including BCC, in the UK is the MDT. It was first recommended by NICE in 2006[37] to be in two forms: the LSMDT and the SSMDT. NICE described in the guidance the types of patients to be referred to each level of MDT, the roles required from the MDT, and the core and the extended membership of each MDT. This guidance was updated in 2010[6] (and is currently under review), the referral process was reviewed in 2015 and the quality standard was published in 2016.[38] A report was published in 2018 by the BAD[39] in response to the NHS England reform of cancer MDT meetings.[40]

The main points that these guidance documents recommend for BCC are:

- To refer for discussion at an LSMDT meeting
    - All patients with high-risk BCCs that involve the excision margins or are recurrent.
    - Patients suitable for Mohs micrographic surgery.
    - Immunocompromised patients (e.g. organ transplant recipients, patients with haematological malignancy or HIV/AIDS) with skin cancers and patients who have Gorlin syndrome or other genetic conditions in which predisposition occurs.

  - All patients with low-risk BCCs that should not be treated in primary care, as per Table 3.

- To refer for discussion at an SSMDT meeting
  - Patients with metastatic BCCs.
  - For periodic review, patients developing skin cancers who are immunocompromised, have Gorlin syndrome or have other genetic predisposition syndromes.
  - Patients who may be eligible for entry into clinical trials.
  - Patients who require adjuvant treatment (where this is shown to be beneficial).

Additionally, the GDG recommends that the following cases be referred to an LSMDT member:

- Low-risk BCC in the absence of a competent GPwER or if the primary care facility is not suitable for surgery (see R2).
- Recurrent BCC with high-risk factors when Mohs micrographic surgery is not appropriate, or the patient or the patient's representative with power of attorney declines it (see R11).
- Patients unsuitable for Mohs micrographic surgery or standard surgical excision but suitable for radiotherapy, and patients who may prefer radiotherapy as an alternative treatment option (see R15, R16 and R17).
- Excised high-risk BCC with a close histological margin (< 1 mm; see R23).
- If deep extension of BCC to underlying tissue (e.g. named nerve, muscle or bone) is suspected, following a CT scan or MRI.

In advanced cases of BCC, consider referral to one or more other MDTs, as clinically appropriate.

7.4. Excision techniques with postoperative margin assessment

7.4.1. Standard surgical excision with predetermined margins

For the indications for standard surgical excision with predetermined surgical margins, please refer to recommendations R3–8, R11, R12, R22 and R23. For a more detailed discussion on the evidence that underpins these recommendations please refer to Appendices D1 and D2 (LETR, pp 62–77 and 84–7; see Supporting Information).

Standard surgical excision is an empirical treatment suitable for the majority of primary BCCs, with reported 5-year recurrence rates of 3–8%;[41–43] higher recurrence rates have been reported in more historical papers.[30,44] Standard surgical excision with complete margin control showed 0·5% recurrence at 5 years for primary tumours and 2·9% at 5 years for recurrent tumours in a single study.[45] For Mohs micrographic surgery, recurrence rates for primary tumours of the head and neck range from 0·3% to 6·5%.[42,46–48] Treating already recurrent tumours is associated with higher subsequent recurrent rates, ranging from 4% to 10%.[42,47,48]

Expertly performed, definitive standard surgical excision can therefore have low recurrence rates. Evidence for clinically significant sparing of tissue, which thereby enables less extensive reconstruction by using complex margin-controlled techniques, is limited.

Evidence from case series involving standard excision margins of 4–5 mm in high-risk BCC (head and neck) reports lower incomplete excision rates (3·74%) compared with excision margins of 3–4 mm (4·10%) or < 4 mm (11·31%) (Appendices C and D for proportional meta-analysis forest plots and LETR discussions, respectively; see Supporting Information). Similarly, evidence from case series involving standard excision margins of 4–5 mm in high-risk BCC (whole body) reports lower incomplete excision rates (3·66%) compared with excision margins of 3–4 mm (4·49%) or < 4 mm (9·72%). Dhepnorrarat *et al.*[49] reported a very high volume (21 677) of BCCs excised; data were collected prospectively over a period of 6 years by a defined group of 25 plastic surgeons in Western Australia which showed an incomplete excision rate of 4·01%, although no reference was made to the margins involved.

Standard surgical excision consists of three stages: (i) excision of the tumour with a predetermined margin of normal-appearing skin beyond the visible edge of the tumour; (ii) surgical repair of the wound; and (iii) subsequent histological analysis of the excised tissue.

For a list of good surgical practice points please refer to the 'other considerations' section in Appendix D1.1 (LETR, pp 78–82; see Supporting Information).

7.4.2. Mohs micrographic surgery

For the indications for Mohs micrographic surgery please refer to the recommendations R5, R9, R10, R13 and Θ1. For a more detailed discussion on the evidence that underpins these recommendations please refer to Appendix D1 (LETR, pp 62–4; see Supporting Information).

All the general good medical advice for standard surgical excision still applies to Mohs micrographic surgery, namely the operator should be qualified and working in an accredited centre for such surgery, with sufficient time allocation, high-standard (theatre) lighting, and patient counselling for informed consent. Recently, the BAD published service guidance and standards for Mohs micrographic surgery performed in the UK.[50]

For key features of Mohs micrographic surgery and the differences in technique from standard surgical excision please refer to the 'other considerations' section in Appendix D1.1 (LETR, pp 78–82; see Supporting Information).

Only one RCT to date has compared Mohs micrographic surgery against standard surgical excision, with only 3 mm margins being used for the latter in the study. The subsequent two publications for the RCT showed the recurrence rates with Mohs micrographic surgery to be lower at both 5-year and 10-year follow-ups; however, this was not statistically significant ($P > 0·05$) for primary, high-risk BCC[43] (after 5 years: Mohs

micrographic surgery recurrence rate 2·5% vs. standard surgical excision 4·1%;[51] after 10 years: 4·4% vs. 12·2%, respectively). With regard to recurrent BCC, the same publications showed that the recurrence rate for Mohs micrographic surgery was statistically significantly better ($P < 0·05$) than for standard surgical excision (after 5 years: Mohs micrographic surgery recurrence rate 2·4% vs. standard surgical excision 12·1%; after 10 years: 3·9% vs. 13·5%, respectively).[43,51]

Mohs micrographic surgery can be considered for all high-risk primary BCCs, and offered for recurrent, high-risk BCC. In such cases, either Mohs micrographic surgery is offered or the wound from standard surgical excision should be kept open for delayed reconstruction until the margins are confirmed clear, by paraffin sections.

7.5. Radiotherapy

For the indications for radiotherapy please refer to recommendations R15–R17. For a more detailed discussion on the evidence that underpins these recommendations please refer to Appendix D1 (LETR, pp 64–6; see Supporting Information).

Primary treatment of BCC with radiotherapy is a well-established, definitive treatment. It is considered an acceptable modality in the previous iteration of the BAD guidelines,[4] as well as in international guidelines such as those of the European Dermatology Forum 2019,[14] the US NCCN 2019,[7] and the American Academy of Dermatology 2018.[12,52]

Standard surgical excision or Mohs micrographic surgery is the usual primary treatment for BCC; however, radiotherapy can be considered on an individual patient basis, especially when older patients may prefer radiotherapy as an alternative treatment option, usually after MDT discussion for high-risk BCCs and usually with a diagnostic biopsy. There is evidence for its role as an alternative primary treatment modality for nodular BCC, particularly in older patients with poorer performance status, in those (or their representative with power of attorney) who decline surgery, in patients for whom surgery may result in significantly adverse cosmetic or functional outcomes, and in patients who may prefer radiotherapy as an alternative treatment option. It may be an effective postoperative treatment for BCC with involved (microscopic or macroscopic) histological margins for which further surgery is inappropriate.[14,53]

When managing BCC with perineural invasion (PNI), an MDT team including a cutaneous surgeon and a radiation oncologist familiar with PNI is recommended. Where there is one or more close or involved margin and PNI, further excision should be offered, or radiotherapy if excision is not feasible. The evidence for the role of adjuvant radiotherapy in a completely excised BCC with PNI is weak.[14,53]

There is a single randomized trial evaluating standard surgical excision vs. radiotherapy for facial BCCs < 4 cm, in 347 patients. The 4-year actuarial failure rate was 0·7% (95% confidence interval 0·1–3·9%) for surgery, and 7·5% (95% confidence interval 4·2–13·1%) for radiotherapy ($P = 0·003$). Patients were assessed for cosmetic result at 4 years, which was rated as 'good' in 87% of those having undergone surgery and 69% for radiotherapy.[54,55]

In retrospective case series, 5-year and 10-year local recurrence rates of 4% and 6%, respectively, were reported in a series of 720 head and neck BCCs,[56] with a 5-year recurrence rate of 4·2% reported in another series of 712 patients.[57] In a systematic review of patients with NMSC treated with hypofractionated radiotherapy (i.e. fraction size > 2 Gy), the local recurrence rate did not exceed 7·9% in 33 of 36 studies with follow-up ranging from 2 to 77 months.[57] However, an older retrospective study of 148 patients with 175 BCCs of different subtypes treated with radiotherapy found an overall 5-year recurrence rate of 15·8%; 86·4% of all recurrences appeared within 3 years following treatment.[58] In the same study, compared with nodular BCC, sclerosing (morphoeic or infiltrative) BCC was a significant risk factor for recurrence after radiotherapy; therefore, surgery is generally preferable for these subtypes.[58] If radiotherapy is used for poorly defined BCCs, then a wider planning margin is advised.[58] Surgery is also preferred to radiotherapy in areas of potential poor healing, particularly the leg,[59] and for BCC invading bone or cartilage and recurrent BCCs that have recurred following radiotherapy.[7,12,14]

The acute complications of radiotherapy include moist and dry desquamation, and acute/erosive dermatitis. The longer-term, cosmetic effects of radiotherapy (e.g. hypopigmentation, telangiectasia, fibrosis; and, rarely, skin, cartilage or bone radionecrosis) may worsen over time, and are likely to be worse with a higher dose per fraction.[60] However, there is growing clinical evidence that hypofractionation (larger than the standard 2–2·5 Gy per fraction) does not compromise cosmesis and is particularly appealing to older or frail patients, as fewer treatments are required. Most guidelines therefore recommend reserving radiotherapy for patients aged 60 years or over.[7] Radiotherapy should also not be used in genetic syndromes predisposing to skin cancers such as Gorlin syndrome and xeroderma pigmentosum, as it can predispose to secondary carcinomas.[7,61–64]

For discussions on radiotherapy regimens please refer to the 'other considerations' section in Appendix D1.1 (LETR, p 82; see Supporting Information).

7.6. Other surgical techniques without postoperative margin assessment

For the indications for other surgical techniques without postoperative margin assessment, please refer to recommendations R18–R20 and Θ2. For a more detailed discussion on the evidence that underpins these recommendations please refer to Appendix D1 (see Supporting Information).

7.6.1. Curettage and cautery

Curettage, in combination with cautery or electrodesiccation, up to three cycles has been used as a treatment modality for many years for BCC.[7,12,14] Although it is an expedient and cost-effective technique for superficial lesions, it does not allow histological margin assessment.[7]

Curettage and cautery undertaken by experienced practitioners for well-defined, low-risk nodular and superficial BCCs produces 5-year recurrence rates of 4–8%.[65,66] If it is used for

high-risk BCC it was reported to have a recurrence rate of 19%,[41] which carries significant morbidity to patients and may make subsequent treatment more complicated and cure more difficult to achieve.

Curettage may be used prior to standard surgical excision to define the extent of tumour margins more accurately[67] (see section 7.4.1), prior to Mohs micrographic surgery[48] (see section 7.4.2), prior to cryosurgery[12] (see section 7.6.2) or prior to PDT[68] (see section 7.7.2).

In the event that the curette enters the subcutaneous fat, curettage should be abandoned, and the wound excised surgically.[7,12,14]

7.6.2. Cryosurgery

Although 'cryotherapy' is a common synonym for 'cryosurgery', the GDG agreed to use the latter term because in the UK, the term 'cryotherapy' often refers to cold therapy for destructive and nondestructive purposes. The term 'cryosurgery' refers to the destruction of BCC using liquid nitrogen specifically.

Cryosurgery with liquid nitrogen spray in freeze–thaw cycles is an effective treatment for selected low-risk, well-defined BCCs.[7,12,14] However, the reported 5-year recurrence rates vary significantly, ranging from 7·5%[65] to 20%.[69] This variability might be a result of wrong patient selection, different techniques and different clinician skills, as reported by a single clinician who treated 7338 patients (primary and recurrent BCC and SCC) by cryosurgery over 30 years with a total recurrence rate of 1%.[70]

Thissen *et al.*[71] compared the cosmetic outcome of cryosurgery with that of standard surgical excision of superficial BCC and reported that both clinicians and patients were in favour of standard surgical excision over cryosurgery. Similarly, in an RCT comparing cryotherapy against methylaminolaevulinate (MAL)-PDT, recurrence rates at 5 years were similar, but cosmetic outcomes were significantly better with MAL-PDT.[69]

7.6.3. Laser therapy

Laser destruction of low-risk superficial or thin nodular BCCs has been employed using several different laser types, including pulsed dye[72,73] and CO_2 laser.[74] The latter study randomized patients to CO_2 laser, standard surgical excision or cryosurgery. Complete remission with CO_2 laser was similar to that with cryosurgery but significantly lower than for surgery, although these data were reported after a follow-up period of only 3 months and so are not sufficient to determine efficiency adequately.

7.7. Nonsurgical

For the indications for nonsurgical treatments please refer to recommendations R14, R18–R20, Θ1 and Θ2. For a more detailed discussion on the evidence that underpins these recommendations please refer to Appendix D1 (LETR, pp 68–72; see Supporting Information).

7.7.1. Topical therapy

Two topical agents are licensed for BCC, namely imiquimod and 5-fluorouracil (5-FU).

Imiquimod. Imiquimod is a toll-like receptor 7 agonist that induces a tumour-directed cellular immune response.[75] Several studies support its use in superficial BCC,[72,76–78] and it is licensed in a regimen of 5 days per week over 6 weeks. Many studies support its efficacy in treating single or multiple small, superficial, low-risk BCCs, particularly those on the trunk and limbs, with two noninferiority RCTs comparing imiquimod to standard surgical excision in low-risk BCC[79,80] and to PDT and topical 5-FU 5% cream.[81,82] In these RCTs, topical imiquimod was inferior to standard surgical excision:[79] 3-year follow-up cure rates were 84% with imiquimod and 98% with standard surgical excision ($P < 0·001$), with comparable data at 5 years:[80] 82·5% for imiquimod and 97·7% for surgery ($P < 0·001$). However, imiquimod was superior to both MAL-PDT and topical 5-FU:[81] 1-year follow-up cure rates were 83·4% with imiquimod, 72·8% with PDT and 80·1% with 5-FU, indicating that topical imiquimod was superior to MAL-PDT and that 5-FU was noninferior to MAL-PDT for treatment of superficial BCC.[79,81] Five-year follow-up data confirmed the superiority of imiquimod over both MAL-PDT and 5-FU, with 5-year BCC-free survival rates of 80·5% for imiquimod, 70·0% for 5-FU 5%, and 62·7% for MAL-PDT.[82]

Arits *et al.*[81] noted that topical treatments are associated with very high rates of local AEs, with up to 56% of patients experiencing severe local skin reactions and discomfort. This is variable between patients and may necessitate alterations to treatment regimens to achieve maximal efficacy without unacceptable side-effects. Around 5% of patients treated with topical imiquimod also experienced systemic flu-like symptoms.[81]

In terms of cosmesis, if the BCC does not recur, then topical therapy is associated with comparable or superior cosmetic outcomes to standard surgical excision at 3 years.[79]

5-Fluorouracil cream. 5-FU, a topical chemotherapeutic agent, is licensed for treatment of superficial BCC in a treatment regimen of once or twice daily for 3–4 weeks.[83] As mentioned above, 5-FU is inferior to imiquimod but is noninferior to MAL-PDT.[79–82] Rates of local AEs are similar to those seen with imiquimod, but flu-like systemic symptoms were not seen with use of 5-FU in one study.[81] One study suggested that 5-FU treatment was associated with higher rates of wound infection than imiquimod treatment.[81]

Other agents. A low-certainty, randomized, vehicle-controlled clinical study involving 94 participants, of whom 62 patients with superficial, nodular, cystic and pigmented BCCs were treated with solasodine glycoalkaloids. This study reported 66% efficacy with solasodine glycoalkaloids, compared with 25% for the vehicle group at the end of an 8-week treatment period, which was reduced to 47% by the

end of the year.[84] The results in this single study are not sufficient to determine the safety and efficacy of the studied cream compared with more established topical agents.

7.7.2. Photodynamic therapy

Topical PDT is a widely studied treatment option for low-risk, **superficial** BCC.[69,81,82,85–87] In these studies, PDT was compared with cryosurgery,[87] standard surgical excision[86] and topical therapy (imiquimod or 5-FU).[81,82,85] The studies showed that PDT was not inferior to cryosurgery, standard surgical excision or 5-FU, while imiquimod was superior to PDT. The cosmetic outcome of PDT was better than with cryosurgery and standard surgical excision but was equal to that of imiquimod or 5-FU.[69,81,82,85,86]

PDT is associated with few AEs, of which some are expected (e.g. pain during and after treatment and an acute local reaction) and some are unexpected, (e.g. urticaria in the treated area, hyper- and hypopigmentation, and rarely, scarring and contact sensitization).[88]

Some studies indicate a possible role for PDT in treating **nodular** BCC, although 5-year follow-up studies indicate efficacy rates of no more than 76% at best:[89] 2-year cure rate of 94% for standard surgical excision and 74% for PDT;[90] 5-year cure rates of 96% and 76%, respectively;[89] 12-month cure rates of 79% and 62%, respectively;[68] 3-year cure rates of 97·7% and 69·7%, respectively;[91] and 5-year cure rates of 98% and 72% for PDT, respectively.[92]

Guidelines regarding use of PDT in BCC can be found in the BAD and British Photodermatology Group updated guidelines for topical PDT.[93]

7.7.3. Hedgehog pathway inhibition

For a more detailed discussion on the evidence that underpins these recommendations please refer to Appendix D1 (LETR, pp 67; see Supporting Information).

Vismodegib and sonidegib are hedgehog pathway inhibitors and specifically target oncogenic smoothened receptors. Both vismodegib and sonidegib are approved by the European Medicines Agency and the US Food and Drug Administration for treatment of adults with laBCC who are not candidates for surgery or radiotherapy, while vismodegib is also approved for patients with mBCC. Currently in the UK, vismodegib has a marketing authorization but did not attain NICE approval for treating symptomatic metastatic BCC in the NHS, whereas sonidegib does not have a marketing authorization.

Vismodegib demonstrated efficacy in patients with laBCC and mBCC in the pivotal ERIVANCE clinical trial.[94–96] Efficacy was confirmed in a subsequent global safety study (STEVIE clinical trial),[97,98] and was also demonstrated in a separate RCT in patients with Gorlin syndrome.[99,100]

In total, 104 patients were treated in ERIVANCE. At 39 months, response rates were 60·3% (laBCC) and 48·5% (mBCC, all partial responses), and median response durations were 14·8 months (mBCC) and 26·2 months (laBCC).[94–96] During treatment, class-specific AEs were common and included muscle spasm, taste alterations, hair loss, fatigue and weight loss. These AEs appeared in the majority of patients and led to treatment discontinuation in 21% of all treated patients. In the primary analysis of STEVIE, 1215 recruited patients were evaluable (1119 laBCC, 96 mBCC). Investigator-assessed response rates were 68·5% for laBCC and 36·9% for mBCC, and the AEs were consistent with those identified in ERIVANCE.[97,98] Treatment was associated with improvement in health-related quality of life.[101]

In patients with Gorlin syndrome, a randomized, placebo-controlled trial showed a significant reduction in the number of new, surgically eligible BCCs on treatment with vismodegib compared with placebo (2 vs. 29 cases per group per year, $P < 0{\cdot}001$).[99,100]

The MIKIE study showed that two intermittent dosing regimens of vismodegib were effective in the control of patients with multiple BCCs, including Gorlin syndrome. The regimen with a shorter induction period of 12 weeks (followed by 8 weeks of placebo alternating with 12 weeks of treatment) showed a similar AE profile to that in the group with a 24-week induction period (followed by 8 weeks of placebo alternating with 8 weeks of treatment).[102]

Studies of neoadjuvant vismodegib in patients with laBCC are promising, especially in the periocular and orbital area followed by Mohs micrographic surgery.[103–105]

Sonidegib, the other smoothened inhibitor, was also shown to be clinically effective in a pivotal prospective randomized double-blinded clinical trial (BOLT).[106,107]

7.7.4. Electrochemotherapy

NICE recognized ECT as an ablative treatment for metastases in the skin from tumours of nonskin origin and melanoma,[108] and in 2014 produced a guidance on ECT for primary BCC and primary SCC.[109] With regard to primary BCC, NICE advised that *'evidence on its efficacy is limited in quantity and quality'*, and that the clinician should *'ensure that patients understand the uncertainty about the procedure's efficacy and why it is being offered as an alternative to other established methods of treatment'*.[109] Since then, four nonrandomized comparative and noncomparative studies, and one RCT have been published.[110–114] The certainty of these studies are generally very low, and none provided additional evidence to update the NICE recommendations in its guidance for treating primary BCC.

Campana *et al.*[115] and Gehl *et al.*[116] produced recommendations and minimal requirements for reporting clinical data on ECT and updated the standard operating procedures for ECT, which, if future trials followed these, would help provide further evidence for clinical practice. For a more detailed discussion on the GDG's decision not to recommend ECT for treating BCC, please refer to Appendix D1 (LETR, pp 73–4; see Supporting Information).

7.7.5. Other treatments

There are other treatments that have been reported in the literature to treat BCC, but they are either historical or currently

have insufficient evidence to recommend their use for treating BCC.

Chemotherapy. Literature on chemotherapy for BCC is old and limited to case reports[7] that would not comply with the guideline's inclusion criteria. Moreover, since the introduction of hedgehog inhibitors, chemotherapy has rarely been used in practice (personal communications).

Systemic immunotherapy. Literature on systemic immunotherapy is fairly new but still limited to a phase II study and case reports. These reports indicate that anti-programmed death-1 (anti-PD-1) drugs, namely pembrolizumab[117,118] and nivolumab,[119,120] might be promising agents to treat advanced BCC, although one[120] of the two reports on nivolumab showed that new superficial and nodular BCCs appeared during successful treatment of a metastatic tumour.

Combination therapy. There were few studies, and of very low certainty, evaluating a number of different combination therapies to treat nodular BCC, such as combinations of diclofenac + calcitriol,[121] imiquimod + Mohs micrographic surgery,[122,123] interferon-α + standard surgical excision,[124] topical PDT + Mohs micrographic surgery[125] and lasers + topical PDT.[126–128] In order to assess such combination therapies, they need to be followed up for at least 5 years.

7.8. Basal cell carcinoma in children and young people

BCC is extremely rare in children under 15 years of age,[129] and when seen is generally in the context of inherited conditions such as Gorlin syndrome (prevalence 1 per 40 000–60 000).[130] Childhood BCC may also be seen in association with xeroderma pigmentosum, Bazex syndrome, Rombo syndrome, albinism, previous radiotherapy and naevus sebaceous.[11,129,131] Sporadic idiopathic BCC in childhood is also reported in the literature, with a total of 107 cases reported worldwide.[129,131] All childhood BCC should be managed within the context of a specialist MDT including specialists experienced in treating skin cancer in children.[130,132]

The first-line treatment option for childhood BCC is surgery, with either standard surgical excision or Mohs micrographic surgery.[129–132] Other treatments described for treating childhood BCC include radiotherapy (contraindicated in inherited BCC syndromes),[14,62,132] topical therapy, curettage and cautery, PDT and cryosurgery.[129–132] However, in view of the high recurrence rates for childhood BCC (18% overall),[131] these treatment options are not recommended.

Vismodegib has proven efficacy in treating BCCs associated with Gorlin syndrome, but its use in children is limited by side-effects, a high recurrence rate and incidence of new tumours on cessation of treatment. In addition, vismodegib is currently not recommended by NICE guidance in the UK.[130,132]

Reducing the risk of future development of BCC should start in childhood with ultraviolet protection, particularly in those with predisposing conditions. Early detection is important, so for children with a high risk of BCC, education on skin surveillance and regular follow-up with a dermatologist are recommended.[14,130–132]

8. Follow-up

Please refer to recommendations R24–R26 and Appendix D3 (pp 87–90; see Supporting Information) . R24 is underpinned by higher-certainty evidence against routinely following up adequately treated BCC, whereas R25 and R26 are recommendations based on GPP. There are many specialties that treat BCCs and other skin cancers, and each specialty will have their own clinics and policies to govern the follow-up process.

The possible reasons for follow-up after initial diagnosis and treatment include (i) detection of local recurrence for tumours at high risk for recurrence, (ii) monitoring of advanced BCC following conservative or palliative treatment, (iii) surveillance for subsequent development of new BCCs and/or other skin cancers and (iv) repeating the advice on BCC verbally and in written format (as mentioned in section 7.1).

At present there is no evidence that follow-up is required for patients with a single, adequately treated low-risk BCC. However, for patients with inadequately treated BCC at high risk of recurrence, for patients with a past history of multiple primary or recurrent BCCs, or for those who are at high risk of developing multiple BCCs (e.g. in the setting of Gorlin syndrome or immunosuppression), then long-term follow-up may be justified. There is no evidence to support how often this should be, but 6-monthly follow-up for the first year, then annually for at least 5 years and possibly up to 10 years or longer may be appropriate. This may need to be more frequent in selected high-risk patients such as those with Gorlin syndrome or immunosuppressed organ transplant recipients. For patients with advanced BCC, follow-up is likely to be required and should be decided as part of management discussions within the SSMDT and on a case-by-case basis.

9. Prevention

Patients with a history of BCC have an increased risk of developing further skin cancers of all types.[133–135] For this reason, advice regarding the avoidance of excessive exposure to ultraviolet radiation, including from sunbeds, and regular skin surveillance is recommended for all patients with BCC. Practical guidance in this regard, including on vitamin D supplementation, is well described in the NICE guidance 'Sunlight exposure: risks and benefits'[136] and in conjunction with another NICE guidance on 'Vitamin D: supplement use in specific population groups'.[137]

Although excessive ultraviolet radiation exposure is strongly associated with the development of BCCs, there is no good evidence for the benefit of sunscreens in preventing further BCC (in contrast to actinic keratosis and cutaneous SCC).[138] Despite the lack of firm evidence for the role of sunscreens in preventing BCC, it is still considered an important part of

general advice on sun protection. Specific agents that have been studied for the chemoprevention of BCC are described below.

Nonsteroidal anti-inflammatory drugs (NSAIDs; other than aspirin): a large RCT found that oral celecoxib 200 mg twice daily significantly reduced the mean number of BCCs in a high-risk population.[139] However, there is a known risk of cardiovascular events with long-term use of cyclooxygenase-2 (COX-2) inhibitors, and therefore routine use in the prevention setting is not currently recommended.

Oral retinoids: acitretin has long been used in transplant/immunocompromised patients with a high keratinocyte tumour burden. Its use is limited due to a high rate of mucocutaneous side-effects and hyperlipidaemia. No large RCTs have been carried out in the nonimmunosuppressed population, although a small study demonstrated that acitretin 25 mg once daily was associated with 25% fewer keratinocyte cancers (both BCC and SCC) compared with placebo.[140] However, the results lacked statistical significance for the study size (designed to pick up a difference of 33% or more).

Oral nicotinamide: an RCT involving nicotinamide 500 mg twice daily in patients with a history of NMSC showed a relative reduction in BCC incidence of 20% at 12 months.[141] This result was modest and not statistically significant, and the reduction in BCC incidence was not maintained upon cessation of the drug. A clinician wishing to advise on oral nicotinamide should highlight to their patients that it gives no more than 20% relative reduction in the number of BCCs, the effect is not long-lasting following treatment cessation, and the evidence is based on only one trial that has not been repeated.

Other oral agents: both α-difluoromethylornithine[142] and selenium[143] have been studied for effects on BCC prevention, but no significant risk reduction has been found.

Topical retinoids: neither tazarotene[144] nor tretinoin[145] has been shown to significantly reduce the risk of BCC.

In conclusion, aside from sun protection[146] and regular skin self-surveillance, which should be recommended for all patients following a diagnosis of BCC, there is some evidence for a small preventative effect of oral acitretin, nicotinamide and non-aspirin NSAIDs. Due to the commitment of lifelong medication and the potential for side-effects, these are likely to be recommended only for those with a history of multiple BCCs.

10. Recommended audit points

All clinicians treating skin cancer should audit their histological concordance and complete excision rate (Appendix L; see Supporting Information). Current examples available for use include:

- For dermatologists who are core MDT members: the British Society for Dermatological Surgery (BSDS) audit tool (https://bsds2020.wpengine.com/wp-content/uploads/2020/10/Dr-Brays-Surgical-Log-Book.zip).
- For primary care clinicians involved in skin cancer surgery: the Community Based Surgery Audit (CBSA) tool (www.rcgp.org.uk/clinical-and-research/our-programmes/quality-improvement/community-based-surgery-audit.aspx), to document all surgically treated cases of NMSC including BCC.
- Other secondary care specialists may have alternative arrangements for auditing their practice.

These tools calculate the statistics while adding the histology results. They present the results for the whole department or for the individual surgical operators in the department.

For all cases of BCC, is there documentation of the following (modified **BSDS audit tool**)?

- Surgeon identity
- Patient identity without any identifiable personal data entry
- Site of lesion
- Primary vs. recurrent lesion
- Type of surgery
- Clinical surgical margins
- Closure
- Growth pattern, deep invasion, perineural invasion and TNM stage
- Histological margin clearance
- Complications
- Follow-up plan

For all cases of BCC managed in primary care, is there documentation of the following (**CBSA audit tool**)?

- Surgeon
- Patient
- Procedure type
- Location of lesion
- Closure
- Histology service usage
- Histological diagnoses
- Comparison of clinical and histological diagnoses
- Histological margin completeness
- Complications
- Management information
    - Waiting time for surgery
    - Waiting time for histology results
    - Consent for surgery
    - Postoperative information
    - Onward referral

Individual operators and units should regularly audit their outcomes, with a target of ≥ 95% complete excision rate being defined as acceptable.[147,148]

11. Stakeholder involvement and peer review

The GDG consisted of representatives from the National Cancer Research Institute (NCRI) Skin Cancer Clinical Studies Group and nonmelanoma skin cancer subgroup (C.A.H.), the RCGP (J.B.), the RCPath (D.N.S.), the Royal College of Radiologists (RCR) (K.F.), the British Association of Oral and Maxillofacial Surgeons (BAOMS) (C.N.), the British Association of

Plastic Reconstructive and Aesthetic Surgeons (BAPRAS) (P.G.B.), the British Society for Dermatological Surgery (BSDS) (R.J.M.), the British Society for Skin Care in Immunosuppressed Individuals (BSSCII) (J.T.L.), the British Dermatological Nursing Group (BDNG) (J.N.) and the Primary Care Dermatological Society (PCDS) (N.S.). The draft document and supporting information were made available to the BAD membership, the RCGP, RCPath, RCR, BAOMS, BAPRAS, BSDS, BSSCII, BDNG, PCDS and British Association of Head & Neck Oncologists (BAHNO), whose feedback was actively considered by the GDG. Following further review, the finalized version was sent for peer review by the Clinical Standards Unit of the BAD, made up of the T&G subcommittee, prior to submission for publication.

12. Limitations of the guideline

This document has been prepared on behalf of the BAD and is based on the best data available when the document was prepared. It is recognized that under certain conditions it may be necessary to deviate from the guidelines and that the results of future studies may require some of the recommendations herein to be changed. Additionally, it is acknowledged that limited cost-effectiveness data in the context of the UK healthcare setting may impact on the availability of a given therapy within the NHS, despite evidence of efficacy. Failure to adhere to these guidelines should not necessarily be considered negligent, nor should adherence to these recommendations constitute a defence against a claim of negligence. Limiting the review to English-language references was a pragmatic decision but the authors recognize this may exclude some important information published in other languages.

13. Plans for guideline revision

The proposed revision for this set of recommendations is scheduled for 2026; where necessary, important interim changes will be updated on the BAD website.

Acknowledgements

We are very grateful to the patient representatives for their input in formulating the clinical questions, ranking of the outcomes, reviewing the evidence and subsequent draft guideline; to clinical oncologist Agata Rembielak; and to all those who commented on the draft during the consultation period.

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Supporting Information

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

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Appendix
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