British Association of Dermatologists *draft* guidelines for the management of people with squamous cell carcinoma *in situ* (Bowen's disease) 2021

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NICE has renewed accreditation of the process used by the British Association of Dermatologists to produce clinical guidelines. The renewed accreditation is valid until 31 May 2026 and applies to guidance produced using the processes described in Updated guidance for writing a British Association of Dermatologists clinical guideline – the adoption of the GRADE methodology 2016. The original accreditation term began on 12 May 2010. More information on accreditation can be viewed at www.nice.org.uk/accreditation. www.nice.org.uk/accreditation.

Footnote:
This is an updated guideline prepared for the British Association of Dermatologists (BAD) Clinical Standards Unit, which includes the Therapy & Guidelines Sub-committee. Members of the Clinical Standards Unit that have contributed are NJ Levell (Chair, Therapy & Guidelines subcommittee); B McDonald (BAD Assistant Honorary Secretary), A Bardham, SL Chua, A

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1.0 Purpose and scope

The overall objective of the guideline is to provide up-to-date, evidence-based recommendations for the management of squamous cell carcinoma *in situ* (SCC *in situ*). The document aims to:

- offer an appraisal of all relevant literature up to September 2019, 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 and in the clinic (see section 3.0), in addition to an updated Patient Information Leaflet (PIL; available on the BAD website, http://www.bad.org.uk/public).

The guideline also reviews erythroplasia of Queyrat (EQ)/penile intraepithelial neoplasia (PIN) and Bowenoid papulosis, which have similar histology and are often diagnosed by dermatologists; however, detailed therapeutic review of these conditions is beyond the scope of this guideline.

1.1 Exclusions

This guideline does not review or offer treatment recommendations for vaginal intraepithelial neoplasia or perianal SCC *in situ.*

2.0 Methodology

This set of guidelines has been developed using the BAD's recommended methodology,[1] further information can be found in Appendix J (see Supplementary Information) with reference to the Appraisal of Guidelines Research and Evaluation (AGREE II) instrument [www.agreetrust.org][2] and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) (http://www.gradeworkingfroup.org). Recommendations were developed for implementation in the UK National Health Service (NHS).

The guideline development group (GDG) consisted of six consultant dermatologists, two dermatology specialist trainees, two patient representatives and a technical team (consisting of a guideline research fellow, an information scientist and 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[3] (see section 2.1 & Appendix A; see Supporting Information).

A systematic literature search of PubMed, MEDLINE, EMBASE and Cochrane databases was conducted by the technical team to identify key articles on SCC *in situ* to September 2019; search terms and strategies are detailed in Appendix K (see supplementary information). Additional references relevant to the topic were also isolated from citations in reviewed literature. Data extraction and critical appraisal, data synthesis, evidence summaries, lists of excluded studies and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram were prepared by the technical team. Overall certainty of the evidence from included studies was rated according to the GRADE system (high, moderate, low or very low).

Recommendations are based on evidence drawn from systematic reviews of the literature pertaining to the clinical questions identified, following discussions with the entire GDG and factoring in all four factors that would affect its strength rating according to the GRADE approach (i.e. balance between desirable and undesirable effects, overall certainty of the evidence, patient values and preferences and resource allocation). All GDG members contributed towards drafting and/or reviewing the narratives and information in the guideline and supporting information documents. When there is insufficient evidence from the literature, informal consensus is reached based on the specialist experience of consultants on the GDG.

The Supporting Information contains the summary of findings with forest plots (Appendix B), tables Linking the Evidence To the Recommendations (LETR) (Appendix C), GRADE evidence profiles indicating the overall certainty of the evidence (Appendix D), summary of included studies (Appendix E), narrative findings for non-comparative studies (Appendices F), PRISMA flow diagram (Appendix G), critical appraisal of included systematic reviews (Appendix H) and list of excluded studies (Appendix I). The strength of recommendation is expressed by the wording and symbols as shown in Table 1.

Strength	**Wording**	**Symbols**	**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 whilst only a small proportion would not; for clinicians, most of their patients would receive the intervention; for policy makers, 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; most 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 policy makers 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 whilst only a small proportion would; for clinicians, most of their patients would *not* receive the intervention.

Table 1: Strength of recommendation ratings

2.1 Clinical Questions and Outcomes

The GDG established two clinical questions pertinent to the scope of the guideline (see Appendix A for full review protocol; see Supporting information). The GDG also established a set of outcome measures of importance to patients for each clinical question, that were agreed with and ranked according to the GRADE methodology[3] by the patient representatives. This uses a 9-point scale with outcomes ranked 9 those the patient representatives considered most important. Outcomes ranked 9, 8 or 7 are critical for decision-making; those ranked 6, 5 or 4 are important but not critical for decision making and those ranked 3, 2 or 1 are the least important for decision making. Data on these outcome measures were extracted from included studies (Appendices B, D & E; see Supporting Information).

Review Question 1: Interventions

In people with SCC *in situ* what are the clinical effectiveness/efficacy, safety and tolerability of available treatments compared with each other or in combination or with placebo/no treatment?

- Clearance (within 6 months) **(9)**
- Sustained clearance/recurrence at 1, 2 or 5 years **(9)**
- Adverse events – serious (e.g. bleeding, severe pain, ulceration) **(8)**
- Quality of life **(8)**
- Cosmetic outcome **(6)**
- Convenience of treatment **(6)**
- Treatment tolerability (e.g. pain) **(4)**
- Adverse events – minor **(3)**

Review Question 2: Rates of cancer

What are the subsequent rates of keratinocyte cancer in people who have had SCC *in situ*?

- Incidence of any keratinocyte cancer (at location of previous SCC *in situ)* in studies with follow-up of ≥6 months since treatment/reference time-point **(9)**
- Incidence of progression outside original location of previous SCC *in situ* **(6)**
- Incidence of malignancy **(6)**

3.0 Summary of recommendations

There are few randomized controls trials (RCTs) other than for photodynamic therapy (PDT) to support the following guidelines for the management of SCC *in situ*.

The following recommendations and ratings were agreed upon unanimously by the core members of the GDG and patient representatives. For further information on the wording used for recommendations and strength of recommendation ratings see Table 1. The evidence for recommendations is based on the studies as listed (for details and discussion of the evidence see Appendices B-G; Supporting Information). The GDG recommendations relating to referral pathways are based on discussion and specialist clinical experience amongst consultants on the GDG, as evidence-based details are not available at the time of writing.

The GDG is aware of the lack of high-quality evidence for some of these recommendations, therefore strong recommendations with an asterisk (*) are based on available evidence, as well as consensus and specialist experience amongst consultants on the GDG. Good practice point (GPP) recommendations are derived from informal consensus amongst consultants on the GDG.

In practice, most dermatologists will instigate treatment without first resorting to a biopsy. In the 'real-world' treatment of SCC *in situ*, clinicians may select several different types of treatment to discuss with a patient. Decisions may be influenced by several factors, such as lesion size and thickness, equipment available, and the potential for poor wound healing (e.g. at sites such as the lower leg). Lesions are considered large if greater than 2 cm, and considered high-risk at periocular and digital (and penile) sites. These considerations should be discussed with the patient, as pertaining to the possible complications and risk of incomplete clearance and/or recurrence.

Treatments are presented in a sequence with the least invasive and topical therapies first, then surgical approaches, and finally treatments that require more complex or expensive equipment that are not widely available.

GENERAL MANAGEMENT

R1 (↑) Consider punch biopsy or diagnostic excision when clinical and dermoscopic features are not sufficient for diagnosis of SCC *in situ.*

R2 (GPP) Curettage may be performed, for both treatment and diagnosis, depending on the clinical scenario and operator judgment. Histology specimens should include the deep margin if an assessment of potentially invasive tumour is required.

R3 (GPP) Provide educational material or a patient information leaflet on SCC *in situ* and for any proposed treatment modality e.g. www.skinhealthinfo.org.uk/a-z-conditions-treatments/.

R4 (GPP) Discharge people with SCC *in situ* following completion of treatment, with education on skin surveillance and sun protection, with advice to return to their general practitioner if recurrence or new skin cancer.

R5 (GPP) Consider following up people with SCC *in situ* on an individual basis based on clinical judgment, factoring in lesion size, treatment modality, anatomical location and immunosuppression.

NO TREATMENT

R6 (GPP) Consider conservative measures in people in poor health and with multiple SCC *in situ* lesions, especially on the lower legs. This includes a moisturiser (preferably urea-based) and skin surveillance, proceeding to biopsy if SCC is suspected.

TOPICAL THERAPIES

R7 (↑↑) Offer topical 5% 5-fluorouracil monotherapy to people with SCC *in situ,* for small lesions (e.g. <2 cm) in low-risk sites, and in those who will not or cannot undergo alternative treatments. Initiate a standard regimen of once or twice daily application for 3-4 weeks. Counsel patients regarding the side effects of local inflammation, ulceration and potential scarring (see **R9**).

R8 (GPP) Consider topical 5% 5-fluorouracil monotherapy in people with SCC *in situ,* for larger lesions in low-risk sites, and in those who will not or cannot undergo treatment with other better-established therapies. Initiate a standard regimen of once or twice daily application for up to 4 weeks. Counsel patients regarding the side effects of local inflammation, ulceration and potential scarring (see **R9**).

R9 (**↑**) Consider biopsy and/or the next treatment option if there has been no response to topical 5-fluorouracil after 4 weeks, once the residual inflammation has settled.

R10 (↑) Consider topical 5% 5-fluorouracil monotherapy in people with SCC *in situ* for larger lesions on poorly healing sites (e.g. the lower legs of older patients) as a practical alternative to surgical treatments. Initiate a standard regimen of twice daily application for up to 4 weeks (see **R9**).

R11 (GPP) Consider topical 5% 5-fluorouracil in immunocompromised people with SCC *in situ*, as a practical treatment for multiple and recurring lesions.

R12 (↑) Consider topical 5% imiquimod in people with SCC *in situ* at low-risk sites, when there is no suitable alternative. Consider once-daily application, three times per week for 4 weeks, although prolonged treatment for 12 weeks may be required. Efficacy may be reduced in immunocompromised people.

R13 (↑) Consider topical imiquimod in people with SCC *in situ* lesions located on the lower legs who are inappropriate for, contraindicated or with inadequate response to topical 5% 5-fluorouracil, PDT, laser, curettage with cautery or surgery (see **R31**).

No recommendation (**Θ**) There is insufficient evidence to recommend tazarotene or ingenol mebutate to treat people with SCC *in situ.* Also, with the loss of the marketing recommendation of the latter, it would not be recommended due to the risk of progression to skin cancer.

CRYOTHERAPY (CRYOSURGERY)

R14 (↑↑) Offer cryotherapy as a first-line treatment option to people with small SCC *in situ* lesions (except for lesions on the lower leg) (see **R15**).

R15 (GPP) Employ a single cryotherapy cycle of freezing for 20-30 seconds, or two cycles of 10-20 seconds, for SCC *in situ* lesions (time begins at the creation of a freezing zone). The duration selected may depend on the device used and anatomical location. Advise patients that cryotherapy may be associated with more discomfort, poorer healing and greater recurrence than curettage with cautery.

R16 (GPP) Consider cryotherapy on an individual basis, in people with SCC *in situ* with larger lesions, and those on the lower leg (see **R15)**. Consider patient factors (age, location, skin health) and discuss the risk of prolonged healing and potential ulceration. The time of freezing may need to be shortened to avoid complications, but is associated with a reduction in effectiveness.

R17 (GPP) Consider cryotherapy as a treatment option for immunocompromised people with SCC *in situ*.

CURETTAGE WITH CAUTERY

R18 (↑↑) Offer curettage with cautery as a first-line treatment option to people with small SCC *in situ* lesions, especially if diagnosis is desirable.

R19 (GPP) Consider curettage with cautery on an individual basis in people with SCC *in situ* with larger lesions. Consider patient factors (age, location, skin health) and discuss the risk of prolonged healing and potential ulceration.

R20 (GPP) Consider curettage with cautery as a treatment option for immunocompromised people with SCC *in situ*.

PDT

R21 (↑↑) Offer PDT as a treatment option to people with SCC *in situ*, particularly for poorly healing or cosmetically sensitive skin sites, multiple lesions and large area lesions.

R22 (GPP) Consider PDT in immunosuppressed people with SCC *in situ*, as an effective, well-tolerated and repeatable treatment for multiple and frequently recurring lesions.

No recommendation (**Θ**) There is insufficient evidence to support the use of daylight PDT as a treatment option for people with SCC *in situ*.

STANDARD SURGICAL EXCISION

R23 (↑↑) Offer standard surgical excision to people with SCC *in situ* if there is diagnostic uncertainty regarding invasive disease.

R24 (↑↑) Offer standard surgical excision (5 mm margin), where anatomically possible, to people with SCC *in situ* where morbidity from surgery is low, or for recurrent or refractory disease.

R25 (GPP) Consider standard surgical excision as a treatment option for immunocompromised people with SCC *in situ*.

No recommendation (**Θ**) There is insufficient evidence to support the use of ultrasonic aspiration to treat people with SCC *in situ.*

MOHS MICROGRAPHIC SURGERY

R26 (↑) Consider Mohs micrographic surgery in people with SCC *in situ* when tissue conservation is important, such as periocular and digital sites.

R27 (GPP) Where Mohs micrographic surgery is not available or not appropriate, consider active treatment with any suitable alternative on an individual basis. This includes standard surgical excision, curettage with cautery, PDT, 5% 5-fluorouracil, 5% imiquimod, laser and cryotherapy. Discuss the risk of functional impairment, including that posed by recurrence and its subsequent treatment.

LASER

R28 (↑) Where this service is available, consider laser treatment in people with SCC *in situ* where other treatments have failed or are not suitable. Ablative CO_2 laser may be more effective than non-ablative Neodymium:YAG.

RADIOTHERAPY

R29 (↑↑) Refer immunocompetent people with SCC *in situ* for consideration for radiotherapy where the lesion is recurrent or refractory to other treatments, or where surgery is not appropriate or associated with high morbidity.

R30 (GPP) Consider referring immunocompetent people with SCC *in situ* for consideration of brachytherapy to treat curved surfaces and areas of poor healing, such as the digit and lower legs.

R31 (↑↑) For immunocompetent people with SCC *in situ* lesions located on the lower legs, use treatments other than radiotherapy (apart from brachytherapy), due to prolonged healing time. Offer topical 5% 5-fluorouracil, PDT, laser, curettage with cautery, or surgery.

R32 (GPP) Reserve radiotherapy for immunocompromised people with SCC *in situ* where the lesion has progressed to invasive SCC

COMBINATION THERAPY

R33 (↑) Consider combination therapy if monotherapy with 5% 5-fluorouracil, 5% imiquimod, PDT, laser, cryotherapy, or curettage with cautery fail, and surgery is not appropriate or associated with excessive morbidity. (See Table 2)

Combination treatments in the literature include:
Cryotherapy and 5% imiquimod
Cryotherapy and 5% 5-fluorouracil
Imiquimod and laser
Laser and 5% 5-fluorouracil
Laser and PDT
Simple shaving and PDT

Table 2: Reported combination treatments (n>5) (See table in Appendix D: Supplementary Information, for full details)

List of future research recommendations

The following list outlines future research recommendations (FRRs).

FRR1 RCTs evaluating topicals, standard surgical excision, curettage with cautery, PDT and cryotherapy.

FRR2 RCTs evaluating **c**ombination treatment.

FRR3 Trials to investigate optimum duration of freezing, number of freeze-thaw cycles, and use of a pre-determined peripheral margin for cryotherapy.

FRR4 Comparison study of laser and curettage with cautery, regarding clearance rate, recurrence and cosmetic outcome.

FRR5 Further trials to investigate the efficacy and safety of treatments in immunocompromised people, in particular, 5% imiquimod and laser.

FRR6 Studies on the effectiveness and complication rates of brachytherapy, including at challenging sites such as the digits and lower legs.

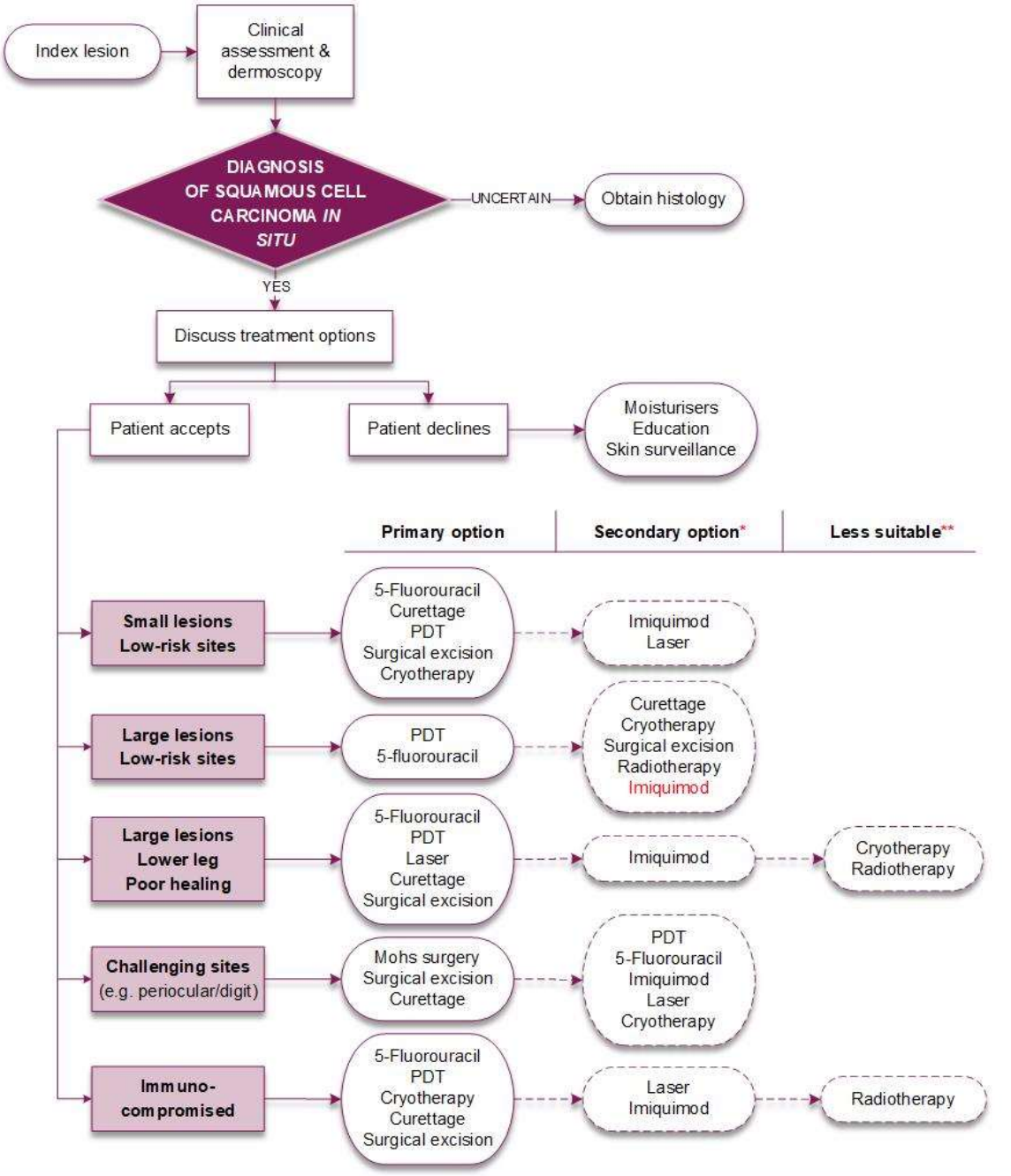
4.0 Algorithm

The recommendations, discussions in the LETR (Appendix C; see Supplementary Information) and consensus specialist experience were used to inform the patient management pathway (Fig. 1).

Fig 1. Patient management pathway – squamous cell carcinoma *in situ*

PATIENT MANAGEMENT PATHWAY – SQUAMOUS CELL CARCINOMA *IN SITU*

Please use in conjunction with the summary of recommendations and discussions in the guideline and supporting information



* Secondary options may be suitable/appropriate as initial management following individualised discussion, depending on the clinical scenario or patient/lesion characteristics

** Less suitable treatments are usually poorer options but may be considered following individualised discussion, depending on the clinical scenario or patient/lesion characteristics

FOLLOW-UP

→ Consider case-by-case follow-up (clinical judgment) factoring in lesion size, treatment modality, anatomical location and immunosuppression

→ Discharge following treatment completion; provide education on skin surveillance; advice to see GP if lesions recur (or a new skin cancer appears)

5.0 Background

5.1 Definition

Bowen's disease is a form of intraepidermal (*in situ*) squamous cell carcinoma (SCC), originally described in 1912,[4] although the original lesions, located on sites that were not sun-exposed were possibly arsenic-induced. A total of six patients were described by Bowen[5,6] and Darier,[7] all with disordered epidermal architecture on histology. In 1911, Queyrat described three men with red lesions limited to the glans penis, applying the French term' erythroplasie'.[8] The histology was identical to that described by Bowen and Darier.

Current practice is to consider Bowen's disease as synonymous with SCC *in situ* for lesions sited on non-genital areas. In line with reduced use of eponyms, we have used the term SCC *in situ* throughout this updated guideline.

5.2 Incidence and aetiology

The most recent data is from the Netherlands, where the incidence rates in 2017 were calculated from a nationwide cancer registry.[9] In men and women these were 68 and 72 cases per 100,000 person-years, respectively, with a statistically significant increase over time. The number of patients with SCC *in situ* treated by dermatologists doubled between 2005 and 2015. In Canada, an annual incidence in men and women of 27.8 and 22.4 per 100,000, respectively, was reported in the period 1996-2000.[10]

Peak incidence of the disease occurs in the seventh decade of life and most studies have shown a slight female preponderance.[9,11-14] The majority of studies report that SCC *in situ* occurs mainly on sun-exposed sites, with more recent studies suggesting the most common being the head and neck (29-54%),[9,13-16] though the lower limb seems to be affected more in females than males.[11,14,17] Older, UK based studies, have reported that the majority of patients (60-85%) have SCC *in situ* on the lower legs which may indicate that the sun exposure pattern is different in countries with lower rates of sunshine.[11,12] Less common variants include pigmented, subungual, periungual, palmar and verrucous SCC *in situ*. Variants exist on genital and perianal locations, and are termed 'penile intraepithelial neoplasia' (PIN) and 'anal intraepithelial neoplasia' (AIN) respectively, each with their own specialist treatment pathway.

Aetiological factors for SCC *in situ* include:

- **Irradiation:** UV light (solar, iatrogenic and sunbeds),[17,18] radiotherapy.
- **Carcinogens:** Arsenic (lesions may arise in sun protected areas).[19]
- **Immunosuppression:** In particular, therapeutic.[20-22]
- **Viral:** HPV DNA has been demonstrated in extragenital SCC *in situ* in varying amounts from 4.8% to 60%.[23-27] A systematic review found HPV detected in 28.3% of 904 extragenital samples, with HPV 16 being the commonest followed by HPV 33.[28] The HPV detection rate was around 3-fold higher in samples from immunosuppressed

patients. HPV 16 may be particularly relevant with regard to development of SCC *in situ* on the hands and feet; being implicated in the majority of palmoplantar and periungual lesions.[29,30] There is an association between HPV, especially HPV 16, and the development of anogenital SCC *in situ*,[23,31,32] but this is by no means conditional for its development.[33] Genital-digital spread is a proposed mechanism linking these sites.

- **Others:** Chronic injury or dermatoses (such as lupus vulgaris or chronic lupus erythematosus) have been implicated.[34-36] Seborrhoeic keratoses have also been associated.[37-40]

6.0 Diagnosis and investigation

6.1 Clinical presentation

SCC *in situ* typically presents as a well-demarcated, asymptomatic, erythematous hyperkeratotic plaque with an irregular border, on sun-exposed sites of a light-skinned person. A pigmented variant accounts for 1.7%-5.5% of cases.[40-42] This has been more frequently described in male patients with darker skin types, and on sun-protected areas such as lower limbs and intertriginous areas.[43-45]

6.2 Investigation

In routine clinical practice the diagnosis is made on clinical grounds. Dermoscopic examination commonly reveals surface scaling, coiled vessels ('glomerular' vessels) and/or red clods (globular' vessels), with the pigmented variant displaying small brown dots and globules.[40,46-50] If there is diagnostic doubt, or confirmation is required before undergoing a certain type of treatment, a punch biopsy can be performed to show full thickness epidermal dysplasia on histology.

If a curette biopsy is performed, this should include the full thickness of the epidermis and dermis, to establish whether there is any invasive disease amounting to a cutaneous SCC. A curettage may therefore be used for both treatment and diagnosis, and perhaps preferable to a punch biopsy in certain clinical settings. This will depend on the suspected differential diagnoses e.g. superficial basal cell carcinoma, the suspicion of invasive malignancy and the skill level of the operator.[51-53] To avoid a scenario where the histology report cannot assess the deep margin and "invasion cannot be excluded", a punch biopsy or excision is best practice in cases of diagnostic doubt.

Histology should be obtained before using a destructive modality, such as laser or radiotherapy, unless the diagnosis is clear. Specimens should be representative of the entire lesion, with large lesions perhaps requiring several punch biopsies or a large incisional biopsy. A repeat biopsy should be considered for lesions resistant to treatment or evolved in clinical appearance.

7.0 Recommended audit points

In the last 20 consecutive patients seen with SCC *in situ*:

1. Is there clear documentation of the therapy type and treatment regimen?
2. Is there clear documentation that a choice of therapy was discussed with the patient?
3. Was a patient information leaflet given on SCC *in situ* and treatment offered?
4. Is there clear documentation that prior to discharge the patient was educated on recurrence?
5. Is there clear documentation that prior to discharge a skin check was performed?
6. Where combinations therapy was used, what were the treatments combined and how were they performed/prescribed. How many sequential treatments did the patient receive for the index lesion and what was the order before surgery?
7. What were the treatment parameters (margins or cycles) used for these treatments (PDT, surgery, cryotherapy) and were any complications experienced?
8. Patient satisfaction and cosmesis with treatment outcome

The audit recommendation of 20 cases per department is to reduce variation in the results due to a single patient and allow benchmarking between different units. However, departments unable to achieve this recommendation may choose to audit all cases seen in the preceding 12 months. See Appendix L; Supplementary Information.

8.0 Stakeholder involvement and peer review

The draft document and Supporting Information was made available to the BAD membership, the British Society for Dermatological Surgery (BSDS), the British Dermatological Nursing Group (BDNG) and the Primary Care Dermatological Society (PCDS). The comments received were actively considered by the GDG. Following further review, the finalised version was sent for peer-review by the Clinical Standards Unit of the BAD (made up of the Therapy & Guidelines Sub-committee) prior to submission for publication.

9.0 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. 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.

10.0 Plans for guideline revision

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

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Declarations of interest

The following interests were declared over the duration of the guideline development:
AJB: (1) invited speaker at educational events – Almirall, Leo Pharma (non-specific); (2) part owner of the trademark Altruist - urea containing cream (specific); **CB**: speaker at educational courses on PDT organized by Galderma (specific); **CAM**: (1) invited speaker – Biofrontera (specific); (2) travel expenses – Galderma (specific); (3) grant/research support – Biofrontera (specific); **ZUH**: grant/research support - Meda Pharmaceuticals, NIHR Clinical Research Network: Cancer (non-specific). **AS, JM, STC, AS, MH, MFMM, LSE**: None

Supporting Information

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

Appendix A: Review Protocol
Appendix B: Forest plots
Appendix C: Linking Evidence To Recommendations (LETR)
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Appendix E: Summary of included studies
Appendix F: Narrative findings for non-comparative studies
Appendix G: Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram – study selection
Appendix H: Critical appraisal of included systematic reviews – AMSTAR 2
Appendix I: Papers excluded from quantitative analysis
Appendix J: Methodology
Appendix K: Search strategy
Appendix L: Audit standards, data items and data collection methodology

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