



Complete Summary

GUIDELINE TITLE

Guidelines for the management of actinic keratoses.

BIBLIOGRAPHIC SOURCE(S)

de Berker D, McGregor JM, Hughes BR, British Association of Dermatologists Therapy Guidelines and Audit. Guidelines for the management of actinic keratoses. Br J Dermatol 2007 Feb;156(2):222-30. [59 references] [PubMed](#)

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Actinic keratoses

GUIDELINE CATEGORY

Management
Treatment

CLINICAL SPECIALTY

Dermatology
Family Practice
Internal Medicine

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To provide recommendations for the management of actinic keratoses

TARGET POPULATION

Patients with actinic keratoses

INTERVENTIONS AND PRACTICES CONSIDERED

1. No therapy
2. Topical therapies
 - Emollient
 - Sun block
 - Salicylic acid
 - 5-Fluorouracil
 - Imiquimod 5% cream
 - Diclofenac gel
 - Tretinoin cream
 - Masoprocol cream
3. Other treatments
 - Cryosurgery
 - Photodynamic therapy
 - Laser, chemical peels and dermabrasion
 - Systemic retinoids

MAJOR OUTCOMES CONSIDERED

- Efficacy of treatment modalities
- Ease of use of treatment modalities
- Morbidity
- Cost-benefit of treatment

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Medline (1966–2004) was the main source of references for this review. Relevant evidence was sought using the search terms "solar keratosis" and "actinic keratosis." Additional and earlier literature was reviewed on the basis of references within post-1966 publications. All articles of apparent relevance were

reviewed independently of the nature of the publication. The National Ambulatory Medical Care Survey (U.S.A.) was used for further data on topical chemotherapy. Papers were reviewed and discussed by the contributors to the British Photobiology Group (BPG) Workshop (see Acknowledgments in the original guideline document).

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Quality of Evidence

I: Evidence obtained from at least one properly designed, randomized controlled trial

II-i: Evidence obtained from well-designed controlled trials without randomization

II-ii: Evidence obtained from well-designed cohort or case-control analytical studies, preferably from more than one centre or research group

II-iii: Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence

III: Opinions of respected authorities based on clinical experience, descriptive studies or reports of expert committees

IV: Evidence inadequate owing to problems of methodology (e.g., sample size, or length of comprehensiveness of follow up, or conflicts in evidence)

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

These guidelines stemmed from a consensus meeting held by the British Photobiology Group (BPG) in 1999. Following one of these meetings one of the authors was invited to draw up guidelines for the management of actinic keratoses (AKs) by the British Association of Dermatologists (BAD) Therapy Guidelines and Audit Subcommittee.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Strength of Recommendations

- A. There is good evidence to support the use of the procedure
- B. There is fair evidence to support the use of the procedure
- C. There is poor evidence to support the use of the procedure
- D. There is fair evidence to support the rejection of the use of the procedure
- E. There is good evidence to support the rejection of the use of the procedure

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Strength of recommendations (A-D) and quality of evidence (I-IV) and are defined at the end of the Major Recommendations field.

Management

Many options are open to patients with actinic keratoses (AKs). The natural history of individual lesions studied in the United Kingdom suggests that treatment is not universally required on the basis of preventing progression into squamous cell carcinoma (SCC). However, others feel that prevention of SCC is the main reason for therapy.

Some AKs have histological features within the spectrum of in-situ skin cancer. They can also represent a cause of symptoms and disfigurement which may be the main determinant of treatment choices. Clinical judgement should discern

which lesions are more likely to represent a risk to the patient's health, but where the likelihood is low, options include no therapy or palliation with emollient or keratolytic agent such as low-strength salicylic acid ointment.

Where active treatment is sought, many modalities of therapy are available (see Table below). Good-quality data on the outcome of these different therapies are available in only a few instances. Treatment of an individual lesion may have a therapeutic effect on surrounding skin, with an effect on overall progression of actinic damage, but this potential benefit has not been quantified. Given the low morbidity and risk of the majority of AKs, the Strength of Recommendation made for treatments by the authors has an element of cost-benefit and risk-benefit included. This is derived from clinical experience in addition to the published evidence.

Topical Therapies

- No therapy **(A, II-ii)** or emollient **(A, I)** is a reasonable option for mild AKs.
- Sun block applied twice daily for 7 months may protect against development of AKs. **(A, I)**
- 5-Fluorouracil (5-FU) cream used twice daily for 6 weeks is effective for up to 12 months in clearance of the majority of AKs. Due to side-effects of soreness, less aggressive regimens are often used, which may be effective, but have not been fully evaluated. **(A, I)**
- Diclofenac gel has moderate efficacy with low morbidity in mild AKs. There are few follow-up data to indicate the duration of benefit. **(B, I)**
- Imiquimod 5% cream is not licensed for AKs, but has been demonstrated to be effective over a 16-week course of treatment but only 8 weeks of follow up. By weight, it is 19 times the cost of 5-fluorouracil. They have similar side effects. **(B, I)**

Additional Topical Therapies

- Salicylic acid ointment **(A, III)**
- Tretinoin cream **(B, I)**
- Masoprocol cream **(C, I)**

In conclusion, there is good evidence that 5% 5-FU cream used twice daily for 3 weeks is effective at reducing AKs on the face and back of hands by about 70% for up to 12 months. There is insufficient randomized controlled trial (RCT) evidence to support or refute the efficacy of alternative regimens and formulations, although one RCT suggests that a single night-time application for 3 months for AKs on the back of the hands is effective. Imiquimod has been more rigorously assessed with modern RCT design and may produce a similar pattern of side-effects and response to 5-FU. Diclofenac gel is a relatively mild agent that reduces the AK count but there are no follow-up data beyond 1 month. Topical tretinoin has some efficacy on the face, with partial clearance of AKs, but may need to be used for up to a year at a time to optimize benefit. Sun block, emollient and 2% salicylic acid ointment BP may reduce the AK count by a similar amount.

Other Treatments

- Cryosurgery is effective for up to 75% of lesions in trials comparing it with photodynamic therapy. It may be particularly superior for thicker lesions, but may leave scars. **(A, I)**
- Photodynamic therapy is effective in up to 91% of AKs in trials comparing it with cryotherapy, with consistently good cosmetic result. It may be particularly good for superficial and confluent AKs, but is likely to be more expensive than most other therapies. It is of particular value where AKs are numerous or when located at sites of poor healing such as the lower leg. **(B, I)**
- There are no studies of curettage or excisional surgery, but both are of value in determining the exact histological nature of proliferative or atypical AKs unresponsive to other therapies, where invasive squamous cell carcinoma is possible.

Additional Other Therapies

- Laser, chemical peels and dermabrasion **(C, III)**
- Systemic retinoids **(B, I)**

Other Considerations

Should actinic keratoses be treated?

There is inadequate evidence to justify treatment of all AKs to try to prevent malignant change. Treatment should be considered on an individual basis according to signs, symptoms, and history. There will be instances where excision is undertaken for diagnostic purposes.

Overall, the data comparing individual treatments are not good enough to justify making a single recommendation. Decisions for an individual patient will be based on the clinical presentation, the efficacy, morbidity, availability and cost of relevant treatments and patient preference.

However, treatment of small numbers of AKs with cryotherapy is currently widely practised by dermatologists, while more extensive AKs are commonly treated with 5-fluorouracil. Due to expense and inconvenience photodynamic therapy (PDT) is probably best reserved for patients with extensive AKs that cannot be controlled with other therapies.

Is there a role for prevention and what works?

AKs are a marker for sun damage and therefore are an indication to increase sun-avoidance measures. There is some evidence that regular use of sunscreen reduces the number of AKs and the risk of SCC.

Should patients with actinic keratoses have follow up?

There are no data concerning the benefit of follow up in patients with AKs. Patients and their carers should be educated regarding changes that suggest malignancy. Those at high risk of nonmelanoma skin cancer, e.g., organ transplant recipients, may warrant follow up; the presence of numerous AKs is an indicator of this risk.

Are there high-risk groups and is their management different?

Patients with multiple and confluent AKs are likely to be at higher risk of nonmelanoma skin cancer, particularly patients with organ transplants who are estimated to have 50 to 100 times the risk of an age- and sex-matched control population. Anecdotal and limited trial data suggest that treatments for AKs in transplant patients are less effective than in the general population, perhaps because AKs are more proliferative and hyperkeratotic in this group, or because new lesions rapidly appear in the treated site. One study in transplant recipients failed to demonstrate a reduction in the development of subsequent skin cancers in those areas of skin previously treated for AKs with PDT.

Cost-benefit of Treatment

Most AKs result in few or no symptoms and are not dangerous. Where there is a wide range of treatments it is necessary to balance the benefits of treatment against side-effects. In many health care systems this calculation will have some element of cost-benefit, where the cost is to the state and the indication must justify the expense. These guidelines are not able to give details on the complex matter of cost-benefit, but it is apparent that some treatments are considerably more expensive than others. Where outcomes are comparable and morbidity of treatment tolerable, we have tended to give a higher strength of recommendation to the cheaper treatment or one that is more easily used in primary care.

Summary of Recommendations

AKs represent a spectrum of clinical complaint and pathology. Most patients can be diagnosed and managed in primary care. In many instances, management may entail little or no medical treatment other than advice on sun avoidance and self-monitoring. Where there is clinical concern or the patient specifically wants treatment, cryosurgery or one of the many topical therapies can be employed taking into consideration the specifics of the situation. If there is diagnostic concern or failure to respond to first-line treatment, a histological specimen, such as obtained at curettage with cautery or formal excision, may be both diagnostic and curative. Where AKs are multiple or confluent, at sites of poor healing or with poor response to standard therapies, photodynamic therapy may be helpful. Such patients may also warrant long-term follow up for the associated increased risk of nonmelanoma skin cancer.

Table. Factors determining choice of active therapy from six main alternatives. The scoring is based on the authors' evaluation of efficacy, ease of use, and cost-benefit

	Cryosurgery	5-FU	Diclofenac	Imiquimod^a	Curettage	PDT	Comments
--	--------------------	-------------	-------------------	------------------------------	------------------	------------	-----------------

Table. Factors determining choice of active therapy from six main alternatives. The scoring is based on the authors' evaluation of efficacy, ease of use, and cost-benefit

	Cryosurgery	5-FU	Diclofenac	Imiquimod^a	Curettage	PDT	Comments
Main characteristics of AKs							
Low number of AKs	****	****	**	**	*	*	
High number of AKs	***	****	***	***	*	***	
Thin AKs	***	****	***	***	*	**	Thin lesions may not always require treatment.
Hypertrophic AKs	**	*	*	*	****	*	Histology may be required. Formal excision may be preferred.
Isolated lesions failing to respond to other therapies	**	*	*	*	****	*	Histology may be required. Formal excision may be preferred.
Confluent recalcitrant AKs, failing other treatments	***	***	*	***	*	***	Certain lesions within a resistant field may require histological assessment.
Location							
Scalp, ears, nose, cheeks, forehead, perioral	****	****	***	****	***	***	
Periorbital	***	*	*	*	***	***	Topical therapies

Table. Factors determining choice of active therapy from six main alternatives. The scoring is based on the authors' evaluation of efficacy, ease of use, and cost-benefit

	Cryosurgery	5-FU	Diclofenac	Imiquimod^a	Curettage	PDT	Comments
							can be difficult to use near mouth and eyes.
Confluent scalp	***	****	***	****	*	****	Pretreatment with 5% salicylic acid ointment may improve outcome.
Below the knee	***	*	**	*	****	****	Poor healing is a particular concern at this site. All modalities can lead to ulceration. Treatment may be combined with advice on elevation and compression bandaging where possible.
Back of hands	****	****	**	*	***	***	Courses of topical therapy may need to be extended and pretreatment with 5% salicylic acid ointment may improve outcome.

Characteristics of patient (rating may be considered in context of clinical need indicated)

Table. Factors determining choice of active therapy from six main alternatives. The scoring is based on the authors' evaluation of efficacy, ease of use, and cost-benefit							
	Cryosurgery	5-FU	Diclofenac	Imiquimod^a	Curettage	PDT	Comments
by characteristic of AK and location)							
Medically dependent or senile	***	**	***	*	*	***	Morbidity of treatment may dictate choice of modality.
Self-reliant	***	****	***	****	*	*	5-FU may be repeated at sites of relapse or new lesions in primary care.
One-off treatment	****	****	*	****	***	***	
Lives far from hospital	***	****	***	****	--	--	May favour treatment that allows monitoring in primary care.
Part of continuous management plan	****	****	***	*	*	***	

****, good treatment; ***, fair treatment, **, can be used depending on circumstances; *, rarely used in these circumstances.

^aImiquimod is not currently licensed for use in the treatment of AKs.

Definitions:

Strength of Recommendations

- A. There is good evidence to support the use of the procedure
- B. There is fair evidence to support the use of the procedure
- C. There is poor evidence to support the use of the procedure
- D. There is fair evidence to support the rejection of the use of the procedure
- E. There is good evidence to support the rejection of the use of the procedure

Quality of Evidence

I: Evidence obtained from at least one properly designed, randomized controlled trial

II-i: Evidence obtained from well-designed controlled trials without randomization

II-ii: Evidence obtained from well-designed cohort or case-control analytical studies, preferably from more than one centre or research group

II-iii: Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence

III: Opinions of respected authorities based on clinical experience, descriptive studies or reports of expert committees

IV: Evidence inadequate owing to problems of methodology (e.g., sample size, or length of comprehensiveness of follow up, or conflicts in evidence)

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is specifically stated for selected recommendations (see "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate prevention and treatment of actinic keratoses
- Prevention of progression to squamous cell carcinoma

POTENTIAL HARMS

- The side-effects of imiquimod cream are similar to 5-fluorouracil (5-FU) with severe erythema (30.6%), scabbing and crusting (29.9%), and erosions or ulceration (10.2%).
- Side effects seen with diclofenac cream include pruritus and rash.
- Photodynamic therapy can be painful and cause local adverse reactions
- Anecdotal evidence over the last 20 years suggests that there can be some considerable morbidity employing systemic retinoids. In addition, there may be a rebound effect once the systemic therapy is stopped.
- Cryosurgery may cause scarring

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

These guidelines have been prepared for dermatologists on behalf of the British Association of Dermatologists (BAD) and reflect the best data available at the time the report was prepared. Caution should be exercised in interpreting the data; the results of future studies may require alteration of the conclusions or recommendations in this report. It may be necessary or even desirable to depart from the guidelines in the interests of specific patients and special circumstances. Just as adherence to the guidelines may not constitute defence against a claim of negligence, so deviation from them should not necessarily be deemed negligent.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Patient Resources

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

de Berker D, McGregor JM, Hughes BR, British Association of Dermatologists Therapy Guidelines and Audit. Guidelines for the management of actinic keratoses. Br J Dermatol 2007 Feb;156(2):222-30. [59 references] [PubMed](#)

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2007 Feb

GUIDELINE DEVELOPER(S)

British Association of Dermatologists - Medical Specialty Society

SOURCE(S) OF FUNDING

British Association of Dermatologists

GUIDELINE COMMITTEE

British Association of Dermatologists Therapy Guidelines and Audit Subcommittee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Authors: D. de Berker, Bristol Dermatology Centre, Bristol Royal Infirmary, Bristol, UK; J.M. McGregor; Department of Dermatology, St Bartholomew's and the London NHS Trust, London, UK; B.R. Hughes, Portsmouth Dermatology Centre, St Mary's Hospital, Milton Road, Portsmouth, UK

British Association of Dermatologists Therapy Guidelines and Audit Subcommittee Members: A.D. Ormerod (*Chairman*); D.J. Eedy; D. Mitchell; F. Humphreys; J. Peters; R. Bull; H. Bell; M. Kouimtzi; S. Jones

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

D. de B., none; J.M.M. has received an honorarium from 3M as an invited member of an advisory board for the treatment of actinic keratoses; B.R.H., none.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [British Association of Dermatologists Web site](#).

AVAILABILITY OF COMPANION DOCUMENTS

A list of Audit Points is provided in the [original guideline document](#).

PATIENT RESOURCES

The following is available:

- Actinic keratosis - also known as solar keratoses. Patient information leaflet. London (England): British Association of Dermatologists; 2007 May. 3 p.

Available from the [British Association of Dermatologists Web site](#).

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI Institute on July 25, 2007. The information was verified by the guideline developer on August 19, 2007.

COPYRIGHT STATEMENT

This NGC summary is based on the original guideline, which is subject to the guideline developer's copyright restrictions.

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.


Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at <http://www.guideline.gov/about/inclusion.aspx>.

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

© 1998-2008 National Guideline Clearinghouse

Date Modified: 4/28/2008

 The image cannot be displayed. Your computer may not have enough memory to open the image, or the image may have been corrupted. Restart your computer, and then open the file again. If the red x still appears, you may have to delete the image and then insert it again.