

Actinic Keratosis, a Chronic, Progressive Disease: Understanding Clinical Gaps to Optimise Patient Management

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Actinic keratosis (AK) is a chronic, progressive disease of the skin that has undergone long-term sun exposure. The affected areas contain visible and subclinical non-visible sun damage resulting in epidermal keratinocyte dysplasia, known by many as 'field cancerisation' (1), which is prone to AKs and sun-related skin cancer (2). Thus, visible AKs are clinical biomarkers for a photo-damaged field with subclinical damage associated with the unpredictable risk of progression to invasive squamous cell carcinoma (iSCC) (3). The aim of this multiexpert opinion article is to provide a discussion succinctly highlighting the clinical gaps for optimal management of AK: the lack of a universal definition and the need for a standardised grade assessment of AK/field cancerisation that also takes into account individual risk.

The prevalence of AK varies from 6–60%, depending on age, phototype and other predisposing risk factors (most notably immunosuppressed status, outdoor workers), and is increasing (1, 4), with a parallel increase in non-melanoma skin cancer (NMSC). AK presents a considerable socioeconomic burden, which will inevitably increase with an aging population (1, 4). To minimise this burden, AK should be recognised and treated, particularly in populations at high risk of NMSC. The goal of therapy should be to eliminate AK/field cancerisation (visible and non-visible subclinical lesions) to minimise risk of AK recurrence and potential progression to iSCC (5), although evidence for the latter is lacking. Some authors in specialised centres have shown the additional value of imaging methods in such management, particularly in visualising the evolution of subclinical lesions, which can be a challenge in current clinical practice (2).

Lesion-directed therapy (e.g. cryotherapy), treats only visible AKs, so field-directed treatment is necessary to treat subclinical damage, reduce AK recurrence rates and potentially minimise the risk of iSCC development (5). Recent guidelines recognise the importance of treating the entire field (5–7). However, cryotherapy alone

remains the standard of care for treating AK patients with multiple lesions. This suggests that education, and growing evidence that treating the field is equally as important as treating visible AKs, will be instrumental in reducing the increasing disease burden. Shifting the treatment paradigm will require understanding the clinical gaps that need addressing.

Firstly, there is a need for a standardised definition of AK field cancerisation in clinical, molecular and histopathological terms. Current guidelines define field cancerisation based on number of AK lesions and presence of surrounding photo-damaged skin (5–7). However, there are wide discrepancies within these criteria (**Table I**). Moreover, experts have voiced concerns over using a definition based on AK counts, as existing evidence suggests that any AK should be considered a marker of field change (8). A clearer and unambiguous definition of field cancerisation that is standardised and reproducible is required to support diagnosis and management, including treatment options and identification of 'red flag' signs of high-risk tumours. Physicians can only manage field cancerisation appropriately if they understand its characteristics and severity.

A second clinical gap is the lack of a reproducible clinical global assessment scale for grading AK/field cancerisation. Current guidelines assess only the presence or absence of AK/field cancerisation, without a severity grading. A global assessment scale should include a clinical description of the key characteristics for each grade of severity to guide effectively identification, diagnosis and treatment decisions.

This clinical grading should be considered alongside modulating risk factors:

- age
- skin phototype
- lifestyle
- occupation
- geographical location
- history of skin cancer
- immunosuppression.

Through clinical grading based on disease severity and individual patient risk factors, a therapeutic algorithm

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Table I. Various definitions of field cancerisation

Guideline	Year	Definition of 'field cancerisation'
International League of Dermatological Societies/European Dermatology Forum	2015 (5)	"At least 6 AK lesions in one body region or field, and contiguous areas of chronic actinic sun damage and hyperkeratosis"
Swiss Registry of Actinic Keratosis Treatment (REAKT) Working Group	2014 (6)	"Two or more AKs on photodamaged skin"
Italian expert consensus for the management of actinic keratosis (AK) in immunocompetent patients	2016 (7)	"...a lesion density $\geq 3/25$ cm ² skin field..."

that enables physicians to make informed treatment decisions would be valuable.

A relevant clinical challenge is the lack of direct evidence to date that AK can progress to iSCC, and that treating AK may prevent the risk of SCC. This is likely to impair the uptake of field therapy despite recommendations by current guidelines.

However, it seems reasonable to advocate field treatment in appropriate patients based on expert clinical judgement supported by:

- a well-established association between AK/field cancerisation and skin cancer (9)
- emerging evidence that field therapies treat field cancerisation (i.e. visible AK lesions and non-visible subclinical lesions) (2), and
- preliminary evidence that field therapies prevent SCC in animal models (10).

In summary, addressing the lack of expert consensus on the definition and grading of AK/field cancerisation is crucial to aid physicians in their decision making and optimise appropriate management of AK.

Aiming to address such a need, the authors propose to undertake:

- a systematic review of the literature on field cancerisation to inform a robust definition
- a global assessment scale for grading AK, which takes into account the entire affected field and not only individual AK lesions.

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