

Assessing the influence of actinic keratosis on patients' quality of life: the AKQoL questionnaire

S. Esmann,¹ G.R. Vinding,¹ K.B. Christensen² and G.B.E. Jemec¹

¹Department of Dermatology, Roskilde Hospital, Health Sciences Faculty, University of Copenhagen, Koegevej 7-13, DK 4000 Roskilde, Denmark

²Department of Biostatistics, University of Copenhagen, Copenhagen, Denmark

Summary

Correspondence

Gabrielle R. Vinding.

E-mail: grv@regionsjaelland.dk

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Conflicts of interest

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Background Limited knowledge is available regarding quality of life in patients with actinic keratosis (AK).

Objectives To develop and validate a disease-specific questionnaire – the Actinic Keratosis Quality of Life questionnaire (AKQoL) – to assess the quality of life of patients with AK.

Methods Based on an extensive literature search and patient interviews, the AKQoL was developed in a stepwise approach. An initial mega-questionnaire was composed and subsequently shortened based on statistical differences between patients and controls. A test–retest was done to establish the reliability and to refine the items further. Rasch analyses were performed on the final questionnaire.

Results Initially, 175 items were tested in a mega-questionnaire. The questionnaires were sent out twice and statistical analyses were made, reducing the number of questions to 18 and 10, respectively. Subsequent inter-item correlations showed that one item had only a weak correlation to the rest of the scale. This was confirmed by the Rasch model and by internal consistency as evaluated by Cronbach's coefficient alpha. Only one item was found to provide a small sex difference. A Bland–Altman plot showed excellent reliability. Items are scored on a standard 4-point Likert scale and summarized in a total score of maximum 27 points. A higher score indicates greater quality of life impairment.

Conclusions A nine-item questionnaire for patients with AK was developed. The AKQoL has three domains covering emotions, function and control and one single global item. The questionnaire's scale structure, the content and face validity, and the reliability have been established.

Hard endpoints such as death are fortunately rare in dermatological diseases. Softer endpoints such as quality of life (QoL) have therefore become an important factor in the assessment of treatment outcome in dermatology over the past 20 years.¹ The estimate or assessment of QoL is however difficult, as it requires an estimate of patients' psychosocial well-being, which is highly context dependent and is therefore affected by the peculiarities of the disease under study, e.g. patients may be more sensible to stigma when their damaged skin is visible and not covered with clothes,² and ultraviolet (UV) sensitivity may be expected to be less problematic in the winter than during the summer.^{3,4} General QoL questionnaires such as the SF-36 do poorly in studies of specific dermatological diseases, and even dermatology-specific questionnaires such as the Dermatology Life Quality Index show limited responsiveness in skin cancer.^{5,6}

Actinic keratosis (AK) is a UV-induced skin disease, which presents as pink, red or brown scaly lesions that may have a sandpappy structure, may itch and feel taut or irritated. AK is commonly interpreted as a marker of excessive UV exposure or as a precursor of skin cancer, although the importance of the disease itself may be neglected by patients. AK is also an illness that is occurring with increased frequency.^{7,8} Although each individual lesion is curable, being diagnosed with AK appears to enhance the risk of developing a new/second AK during the next 12 months threefold to 60%.⁹ Taking into account the high prevalence, frequent occurrence of new lesions and the visibility of AK, it may therefore be speculated that the disease could be perceived as a chronic recurrent skin disease by the patients. The Veterans Affairs Topical Tretinoin Chemoprevention (VATTC) group suggests the term 'actinic neoplasia syndrome' to describe the various manifestations of

chronic UV damage, i.e. for persons who 'have a chronic illness consequent to ultraviolet irradiation, associated with various manifestations including neoplasms such as BCC [basal cell carcinoma], SCC [squamous cell carcinoma] and AKs as well as other signs of photodamage (e.g. solar elastosis)',¹⁰

A change of patients' habits concerning sun exposure is a necessary part of therapy.¹¹ If the concept of AK as a more chronic disorder is accepted, it implies the need to establish disease-specific QoL measures in order, for example, to characterize patient subpopulations and assess the outcome of various interventions.

The present article describes the development of the nine-question Actinic Keratosis Quality of Life (AKQoL) questionnaire, a QoL instrument for adults with AK.

Materials and methods

Study population

Patients with a diagnosis of AK were randomly selected at the Department of Dermatology, Roskilde Hospital and at dermatology clinics in Zealand. Only patients with fluency in written and spoken Danish, age > 18 years, and sufficient physical and mental capacity to comprehend the questions were included (Fig. 1).

Item generation and selection

Literature review

A literature review was carried out covering AK, available treatments and the impact of AK on daily life and QoL (general and disease-specific). A great variety of questionnaires covering dermatological diseases were found, but no questionnaire with focus on AK was available. A similar study on non-melanoma skin cancer (NMSC) has however been published since the completion of this study.¹²

Interviews

In order to develop a questionnaire covering aspects of daily life of importance for patients, open and semistructured interviews were carried out with patients who had AK on their face. Three women and three men took part in the single person interviews. Group interviews were performed as two initial semistructured group interviews and a third, structured, confirmative group interview. The group interviews had two, five and two participants, respectively. In addition, two specialist nurses treating patients with AK with photodynamic therapy (PDT) were interviewed. The interviews provided a list of topics that could be arranged and developed as questions.

Item reduction

The initial, large questionnaire containing 175 questions was sent to 30 patients with AK and to a healthy control group

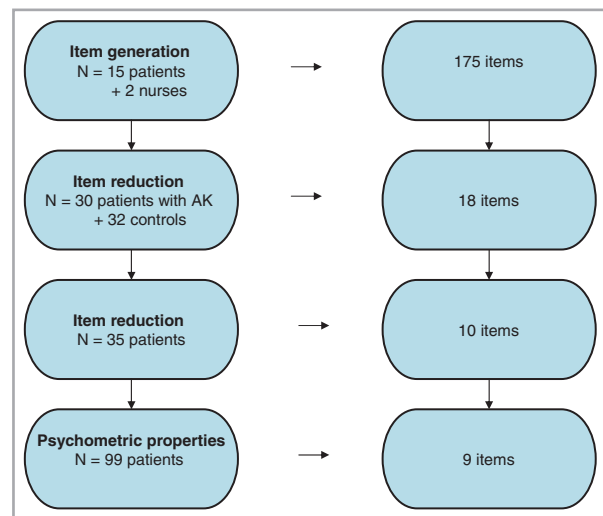


Fig 1. Flowchart of participants and number of items.

consisting of persons without known skin diseases ($n = 32$) in psychomotor-training lessons or among patients with high blood pressure.

Items for further study were selected based on two criteria: a statistically significant difference (SSD) in score between cases and healthy controls and the highest coefficient of variation (COV). By combining SSD and COV it was hoped that the questionnaire would be able to identify differences dynamically, i.e. not only would differences be found, but the magnitude of the response would be sensitive enough to identify graduations. This yielded an 18-item questionnaire.

For practical purposes it was decided to make a further reduction and the reduced questionnaire was sent to 35 patients with AK. The statistical procedure was repeated using the same criteria and furthermore all items were looked at one by one and discussed among the authors.

Scale structure and psychometric evaluation

To ensure the scale structure and psychometric evaluation the resultant 10-item questionnaire was handed out to 105 patients, and 1 week later the questionnaire was sent to the same 105 patients. To estimate the severity of the AK a patients' rating of the seriousness of the AK (on a numeric scale of 1–10) was added. The 10-item questionnaire was tested/retested on persons with AK during the period November 2005 to April 2006 in order to measure the questionnaire's reliability. No quantitative data were available for the *a priori* calculation of sample size. The sample size was therefore based on a general estimate of sample sizes used in similar studies in the literature.¹³

To establish further content validity the AKQoL was handed to 18 patients. The patients were able to pose questions and comments as one of the authors (G.V.) was present all the time.

Statistical analysis

For item reduction two criteria were used: SSD in score between cases and healthy controls and the highest COV.

We computed the three domain scores and computed Spearman's rank correlations. These were compared with what would be expected under the null hypothesis of unidimensionality by simulation of 1000 datasets under the hypothesis, computing rank correlations in each one and comparing the range of simulated rank correlations. The Martin-Löf statistic¹⁴ and a test based on observed and expected gamma coefficients implemented in the computer program DIGRAM¹⁵ were used for a formal test of dimensionality.

We used the Rasch model^{16,17} to validate the scale. The Rasch model places items and respondents on the same underlying scale and can be interpreted using the probability of responses '0', '1', '2' and '3' as a function of the underlying latent variable. An example is shown in Figure 2, in which vertical dashed lines indicate the points where probabilities of adjacent response categories are equal. Using the Rasch model we evaluated whether observed and expected item scores differed. We also compared the location of the items with the location of the answers.

Reliability was measured by test-retest using a Bland-Altman plot. Furthermore, internal consistency was measured by Cronbach's coefficient alpha. An alpha range of 0.7–0.9 was considered acceptable, as a higher alpha score can indicate item redundancy. Inter-item correlation was measured using Spearman's rank correlation coefficients.

We analysed the data using SAS[®] software (SAS Institute Inc., Cary, NC, U.S.A.) version 9.2 and the computer program DIGRAM.¹⁵

Ethical considerations

According to the rules and regulations of the Danish Scientific Ethical Committee the study needed no approval, but the study was approved by the Danish Data Protection Agency.

We also obtained informed consent from participants. The aims of the study were explained and participants were assured of the possibility of unconditional withdrawal from the study.

Results

Item generation

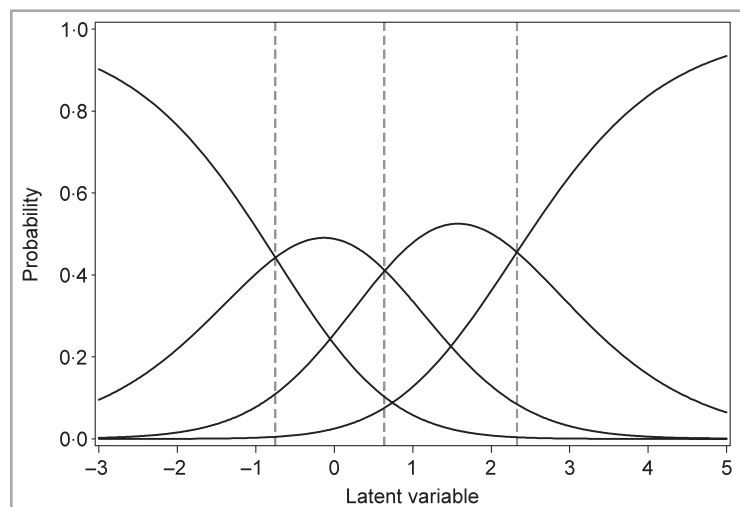
The patients ($n = 15$; nine women, six men; median age 61 years, range 52–85) expressed series of concerns regarding AK, which affected their QoL: the way to act in the sun, a changed appearance, the emotional reaction on the diagnosis of AK, the seriousness of the disease, control of the disease and the sense of illness due to AK. These have been discussed in greater detail in an earlier article.¹⁸ The interviews generated a list of topics that could be arranged and developed as questions. The initial questionnaire had 58 main topics with a variety of subquestions representing, in all, 175 items. The characteristics of the preliminary questionnaire were unconditional and comprehensive, disease specific and including all mentioned topics.

The questions included, for example demographics, emotions, daily life, appearance, cause and treatment of AK, compliance and guilt.

Item reduction

The initial questionnaire was sent to 30 patients with AK and returned by 27 (90%) (16 women and 11 men, median age 59.3 years, range 50–66), and it was sent to a control group of 32 individuals of whom 29 (91%) returned the questionnaire (17 women and 12 men, median age 65.1 years, range 52–78). After statistical analysis, an 18-item version of the questionnaire was obtained. To make a further reduction, the reduced questionnaire was sent to 35 patients and returned by 31 (89%) (19 women and 12 men, median age 61 years, range 47–82).

Fig 2. Example of item characteristic curves from the Rasch model for one of the nine Actinic Keratosis Quality of Life questionnaire items; items and patients placed on the same underlying scale. The probability of responses '0', '1', '2', and '3' as a function of the underlying latent variable; vertical dashed lines indicate the points where probabilities of adjacent response categories are equal.



The statistical procedure was repeated, using the same criteria. Furthermore, possible ambiguous and or redundant questions were sorted out following discussion by the authors (S.E. and G.B.E.J.) and this led to a 10-item version of the questionnaire. Two experts reviewed and rated the items as to its general theme, finding indication of three domains – emotions, function and control – and a global item (item 3).

Testing the psychometric properties

The 10-item questionnaire was handed out to 105 outpatients. The questionnaire was answered outright giving a response rate of 100%. After 1 week the questionnaire was sent to the same 105 patients. Ninety-nine patients (94%) returned the questionnaire (50 women and 49 men), mean age 69 years (range 41–86).

The inter-item correlations showed that item 10 did not correlate well with the rest of the items on the scale. Removing this item still made the rest of the items correlate well with each other and with the total score (Table 1).

The Rasch model confirmed that item 10 had only a weak consistency with the rest of the scale, because observed item scores differed from the expected item scores and it was decided to delete one item due to difficult scoring. For the remaining items there was no discrepancy between the observed and the expected item scores (an example is shown in Fig. 3).

Figure 4 shows the location of the subjects (top panel) and the location of the items (bottom panel) and illustrates that the items are well suited for the population.

We tested the differential item function and only different sex in question 5 was found to give systematically different answers on a given item. The difference between women and men who had the same total score was 0.35 (95% confidence interval 0.08–0.61). Only one out of the 105 patients had a minimum score of 0 and only one had a maximum score of 27, indicating that floor and ceiling effects were very low. The total mean score was 9.5 (SD 4.9).

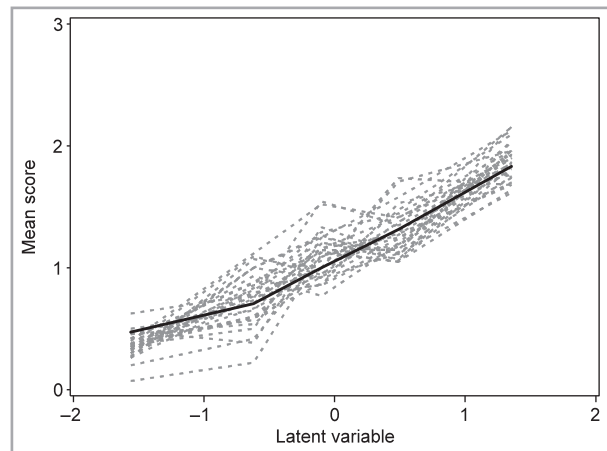


Fig 3. Observed and expected item mean scores for one of the nine Actinic Keratosis Quality of Life questionnaire items.

For internal reliability Cronbach's alpha coefficient was 0.77 for all 10 items. Removing item 10 improved alpha to 0.81. The reliability was tested using the Bland–Altman plot (Fig. 5) showing excellent reliability. Spearman's rank correlation 0.94 ($P < 0.0001$) (items 1–9).

The three domain scores appeared to be highly correlated (Table 2). Testing unidimensionality using the Martin-Löf statistic did not provide evidence against the hypothesis that all items measure the same latent variable. For function (domain 1) and emotions (domain 2) the Martin-Löf test statistic was 52.2 ($df = 80$, $P = 0.99$), for function (domain 1) and control (domain 3) the Martin-Löf statistic was 39.1 ($df = 53$, $P = 0.92$) and for emotions (domain 2) and control (domain 3) the Martin-Löf statistic was 47.3 ($df = 53$, $P = 0.70$). The test based on observed and expected gamma coefficients implemented in the computer program DIGRAM yielded the same conclusion (results not shown).

We finally took a further look at the patients' rating of the seriousness of the AK ['The severity of my sun damaged

Table 1 Inter-item correlations and correlation between each item and total scale score

Scale with items 1–10			Scale with items 1–9		
Item	With single items (lowest and highest correlation)	Total score correlation	Item	With single items (lowest and highest correlation)	Total score correlation
1	0.07–0.61	0.41	1	0.08–0.42	0.42
2	0.08–0.47	0.52	2	0.19–0.47	0.53
3	0.06–0.58	0.64	3	0.12–0.58	0.66
4	0.04–0.51	0.57	4	0.22–0.51	0.59
5	–0.04–0.51	0.43	5	0.08–0.51	0.46
6	0.10–0.61	0.65	6	0.26–0.61	0.66
7	0.08–0.47	0.56	7	0.29–0.47	0.57
8	0.19–0.61	0.57	8	0.19–0.61	0.56
9	0.09–0.36	0.40	9	0.09–0.36	0.35
10	–0.04–0.34	0.16			

Values are Spearman's correlation coefficients.

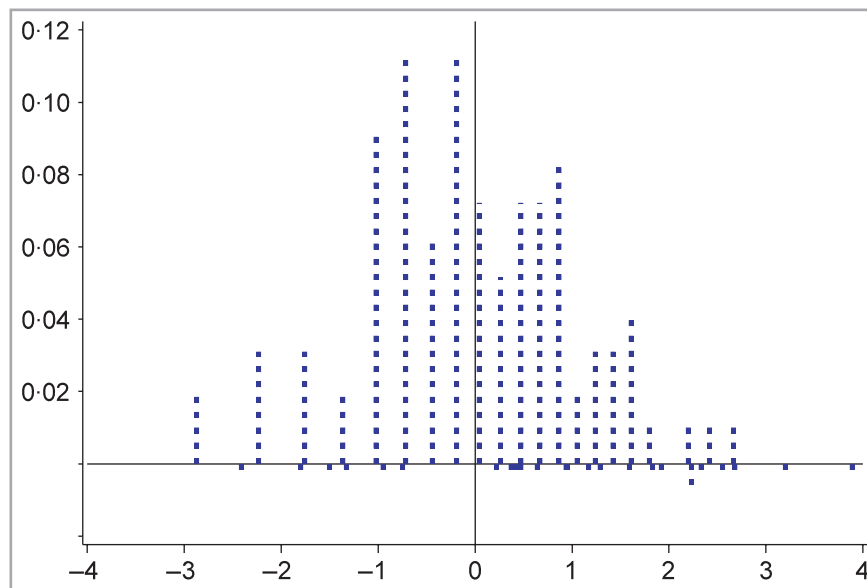


Fig 4. Wright map: the location of the persons (top panel) and the location of the items (bottom panel).

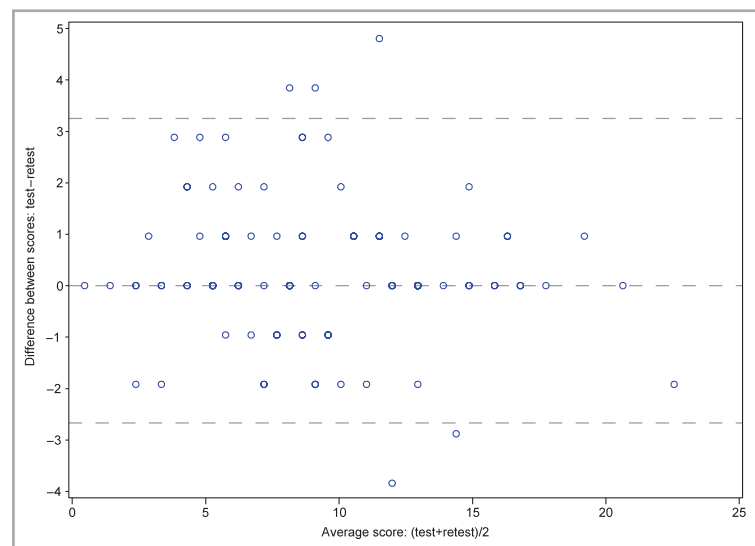


Fig 5. A Bland-Altman plot showing reliability with agreement between test and retest (after 1 week). Note: Solid line denotes group mean difference between test and retest; dotted lines denote 95% limits of agreement (mean difference \pm 1.96 SD).

skin during the last week has been: (choose a number on a scale from 1 to 10, where 1 is mild and 10 is serious)']. Interviews with patients indicated that this question was often misunderstood. In addition it was frequently left unanswered and in consequence it was decided to delete this question.

Missing answers

There were two missing answers among the 10 questions in the first test of the final questionnaire. In the second test, 1 week later, there were five missing answers. The missing answers figured randomly with only one question having two missing answers (Q4). Other involved questions

were Q2, Q3, Q6, Q9, Q10, each with only one missing answer.

The final questionnaire

The final nine-item AKQoL questionnaire (see Supporting information) has three subscales/domains: function (items 1, 8 and 9), emotions (items 2, 4 and 6) and control (items 5 and 7) and one single global item (item 3). The questionnaire reflects personal daily life, personal view of QoL, social life, emotional life and control of life. A standard 4-point Likert scale is used in the scoring of the questionnaires. This gives an answer of either positive or negative character, as there is no middle option. The total score ranges from 0 to 27. The

Table 2 Observed rank correlations between domains

	Domain 1: function	Domain 2: emotions	Domain 3: control
Domain 1: function	1.000	0.530	0.427
Domain 2: emotions	0.530	1.000	0.622
Domain 3: control	0.427	0.622	1.000
Spearman's rank correlations.			

higher the score, the more severe impairment. It takes about 2 min to complete the questionnaire.

Discussion

The AKQoL questionnaire is derived from the concerns expressed by patients. The AKQoL holds nine questions concerning: emotions (fear, guilt, shame, worry and irritation/annoyance), personal view of QoL, social life, appearance and control. The final nine-question version was developed following significant item reduction and testing to suggest its validity. Rasch analysis indicates that the questions may reflect the domains: function, emotions and control.

As mentioned above, a similar questionnaire to the AKQoL questionnaire has been developed recently, with focus on surgery of NMSC.^{5,13} Through the Skin Cancer Index (SCI) Rhee *et al.*⁵ have suggested a tool to measure NMSC-associated QoL. The SCI covers 15 items with the domains: emotions, social and appearance. Both the SCI and AKQoL cover emotional aspects such as anxiousness and frustration. In the SCI, the emotional focus is on the symptoms of the disease, i.e. a possible worsening, the size of the scar, how family members will be affected. In comparison, the AKQoL has a focus on fear of worsening, and on the more existential point of view (question 2, reflecting on important things in life). For most people it is natural to concentrate the thoughts on issues concerning life and death if they get a life-threatening disease. AK is not life-threatening, but being told about AK as a marker of increased risk of developing skin cancer may be associated with an increased focus on the risk of death – an existential topic. Many patients find existential issues relevant.

In the SCI questionnaire, social life is described through questions concerning social contact and questions and comments related to skin cancer. In the AKQoL, the focus is on the patient's wish to hide the disease. It relates to appearance, but also to preventing questions and to the risk of stigmatization. It is hypothesized that the difference may be influenced by the choice of treatment in the sample studied. The SCI was developed in patients undergoing Mohs surgery, whereas the AKQoL was developed in patients primarily undergoing non-invasive therapy such as imiquimod or PDT.

Initially, there were more questions in the reduced AKQoL considering social contacts and other peoples' attitudes. Through the interviews it was shown that other people sometimes want to pay special attention to the patient with AK, e.g. by interfering with the patient's exposure to sunshine.¹⁸ Also,

questions considering family worry were originally contained in an earlier version of the AKQoL. Both types of question were left out during the reduction from 18 to 10 items through discussion among the authors (S.E./G.B.E.J.), as they seemed to have less relevance to patients with AK than other questions.

In contrast to SCI, the AKQoL includes questions regarding control of life (Q7) and inconvenience resulting from prevention (Q8). These topics were highlighted in the interviews. Control of life is a general issue of importance for most people and can be disturbed by illness. This can be transferred to the way the patients act (function) in the sun and has been shown to be of great importance to the patients in our interviews.

One of the few quantitative aspects of AK and QoL that has been studied is the impact of AK count. Based on Skindex-29 and six supplementary items the VATTC Trial group¹⁰ found that higher AK count and past use of topical 5-fluorouracil (5-FU) were predictors of worse QoL. Another report looked at QoL and increase in AK count prospectively, 12, 24 and 36 months later¹⁹ and here, an increase in the number of AKs did not appear to be correlated with changes in QoL. These results were based on a severely sun-damaged population of older male veterans with multiple tumours and are therefore difficult to generalize to other populations. They do however support the need for an illness-specific tool to characterize different populations.

Limitations of the AKQoL include the possible cultural bias when used in other cultures, the use of information that can be provided only by informed patients and the interdependency between sunny weather and the scores. Some of the questions refer to actions in the sun and if the weather has been cloudy during the past week the questions may be perceived to be of less importance.

The above data suggest that the AKQoL truthfully reflects patients' concerns regarding AK. We expect the questionnaire to be a valuable tool in the daily clinic as well as in research, where it can be used, for example, to classify subpopulations of patients, stratify patients in studies or assess the outcome of a range of interventions aimed at helping patients with AKs.

What's already known about this topic?

- Qualitative studies have shown that actinic keratosis (AK) influences quality of life (QoL) negatively.
- General QoL questionnaires do not seem to capture the full impact of AK.
- Patients' self-reported outcomes are increasingly used in studies.

What does this study add?

- The study provides a specific QoL questionnaire for patients with AK.
- Three domains seem to be particularly important for patients with AK: function, emotions and control.

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Supporting Information

Additional supporting information may be found in the online version of this article.

Data S1 Actinic Keratosis Quality of Life questionnaire – provisional translation.

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