Quality of life in non-melanoma skin cancer

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ABSTRACT

Basal cell carcinoma and squamous cell carcinoma are the most common malignancies and are classified under the umbrella of non-melanoma skin cancer (NMSC). NMSC exerts a small but appreciable decrement in quality of life (QOL). The impact posed may arise from the tumour itself or as a result of treatment, and through symptoms, functional limitations, cosmetic burden and auxiliary considerations such as cost and disturbance to the activities of daily living. Researchers have evaluated this burden using a variety of outcome measures including generic, dermatology-specific and disease-specific instruments. The skin cancer index represents a promising disease-specific patient-reported outcome measure in this setting. To overcome some of the constraints inherent to disease-specific instruments, and to allow comparisons with other diseases, utility weightings have been developed. Utility weightings represent a cardinal measure for a specific health status and are established through methods such as the standard gamble, willingness-to-pay and time trade-off, and have also been employed to generate utility weightings for NMSC. Utilities are becoming increasingly important as a means of comparing health states across medicine and are of particular importance from a health-care policy perspective as they are used for resource allocation. The small but definite impact on the individual’s QOL posed by NMSC should be a clinical consideration for physicians and it should be recognised by researchers as a potential outcome measure.

Key words: basal cell carcinoma, quality of life, Skindex, skin cancer index, squamous cell carcinoma, time trade-off, utility, utility weighting, willingness to pay.

INTRODUCTION

Health-related quality of life (QOL) has been defined as the ‘perception of the effects of illness and treatment on the physical, psychological, and social aspects of life’1 and it is becoming increasingly recognised as an important therapeutic outcome in dermatology.2–4 Non-melanoma skin cancer (NMSC) is the most common type of human tumour and, while it infrequently poses a mortality risk, it nevertheless has the capacity to exert a detrimental effect on an individual’s QOL.5 The impact on QOL comes from the tumour itself, from the intervention and from the sequelae after the treatment. It is important to consider that many NMSC appear on the face or visible areas of the skin.6,7 The tumours themselves may be symptomatic, with bleeding, pain and pruritus, and they can cause functional limitations.

Abbreviations:

aBCC advanced basal cell carcinoma
AK actinic keratoses
BCC basal cell carcinoma
DLQI dermatology life quality index
EDC electrodesication and curettage
FACT-G functional assessment of cancer therapy–general
HADS hospital anxiety and depression scale
IPQ illness perception questionnaire
MMS Mohs micrographic surgery
MNSC non-melanoma skin cancer
QOL quality of life
SCC squamous cell carcinoma
SF-36 short form 36-item health survey
SKI skin cancer index
TTO time trade-off
UKSIP UK sickness impact profile
VAS visual analogue scale
WTP willingness to pay

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and cosmetic concerns. Most NMSC are treated with surgery, disrupting the normal activities of daily living, and have a financial impact, and repeated treatments may be needed in the setting of incomplete surgical margins or recurrence. Following treatment, there are cosmetic and functional sequela from scarring that can affect psychosocial function and patients often develop further NMSC, compounding the insult.6 Over the past 20 years several studies have attempted to capture the impact of NMSC on an individual's QOL, identifying physical deformity, cosmesis and psychosocial function as important domains affected.2,9,10 QOL questionnaires have been used as an evaluation tool to quantify a particular health problem as well as utility weightings that quantify a preference for a particular health outcome.4 As they facilitate comparisons between different diseases, utility weighting instruments have become valuable in health–care-related decision-making.11–12 Objectively assessing the impact of NMSC has become valuable in health–care-related decision-making. Between different diseases, utility weighting instruments have become valuable in health–care-related decision-making. However, the applicability of a QOL instrument is inversely proportional to its sensitivity and, accordingly, generic instruments may not identify the QOL issues specific to a particular pathology.13 Particularly in the setting of clinical trials, it is necessary to employ measures that are capable of detecting changes in a given outcome and, accordingly, more sensitive instruments have been developed. Dermatology-specific health status measures such as the dermatology life quality index (DLQI)21 and the Skindex accordingly tend to be more comprehensive, as they address issues specific to skin pathologies and allow comparisons between different dermatoses. However, disease-specific instruments are the most sensitive for evaluating QOL for a particular disease, though the results from these instruments cannot be compared to those of other conditions. Consequently, researchers tend to couple multiple health status instruments to obtain maximal sensitivity and comparability.4,22

The burden of NMSC on QOL was first investigated by Blackford and colleagues15 in a cohort of 57 English patients with clinically diagnosed basal cell carcinoma (BCC). Patients completed the UKSIP20 and the DLQI21 at initial presentation, then at 1 week and 3 months post-treatment. There was no significant difference in QOL scores with time, nor according to the treatment employed or the size of the lesion removed. The authors concluded that BCC has little impact on QOL, with QOL scores at baseline, 1 week and 3 months, comparable to that of the general population (mean UKSIP 0.4, 0.7, 0.15%; mean DLQI 5, 9, 1%, respectively). While Blackford and colleagues’ study was limited by small patient numbers, it showed that these instruments had limited overall sensitivity and sensitivity to change, and were not adequate to detect the impact on QOL of NMSC.

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### Table 1 Quality of life instruments in non-melanoma skin cancer

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BCC, basal cell carcinoma; DLQI, dermatology life quality index; FACT-G, functional assessment of cancer therapy–general; HADS, hospital anxiety and depression scale; IPO, illness perception questionnaire; NMSC, non-melanoma skin cancer; QOL, quality of life; SF-36, short form 36-item health survey; SKI, skin cancer index; UKSIP, UK sickness impact profile; VAS, visual analogue scale.

### QUALITY OF LIFE INSTRUMENTS

Health status instruments aim to capture the impact on an individual’s QOL of a particular disease and are broadly classified as generic, dermatology specific or disease-specific.4 Each of these has been employed in NMSC (Table 1). Generic instruments, such as the medical outcomes short form 36-item health survey (SF-36),19 and the UK sickness impact profile (UKSIP)20 are not specific to any given pathology, allowing them to be employed across the medical field, thus facilitating comparisons between a broad range of diseases. However, the applicability of a QOL instrument is inversely proportional to its sensitivity and, accordingly, generic instruments may not identify the QOL issues specific to a particular pathology.4 Particularly in the setting of clinical trials, it is necessary to employ measures that are capable of detecting changes in a given outcome and, accordingly, more sensitive instruments have been developed. Dermatology-specific health status measures such as the dermatology life quality index (DLQI)21 and the Skindex3 accordingly tend to be more comprehensive, as they address issues specific to skin pathologies and allow comparisons between different dermatoses. However, disease-specific instruments are the most sensitive for evaluating QOL for a particular disease, though the results from these instruments cannot be compared to those of other conditions. Consequently, researchers tend to couple multiple health status instruments to obtain maximal sensitivity and comparability.4,22

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In parallel, Steinbauer and colleagues\textsuperscript{14} investigated QOL in 52 NMSC patients using the German version of the DLQI. The authors demonstrated QOL impairment principally in the symptoms and feelings, daily activities, and leisure activities subscales, consistent with the findings of Blackford and colleagues.\textsuperscript{13} Several parameters, such as occupational impairment, sporting activity and household work, were marked as not relevant, suggesting that the DLQI lacks sensitivity with respect to NMSC. While the overall findings suggested that NMSC exerts a minimal impact on QOL, 51% of patients reported a moderate to strong impairment of QOL, reinforcing the need for a more comprehensive instrument for NMSC patients.

Chren’s group conducted a prospective cohort study of 655 patients with NMSC, evaluating QOL outcomes electrodessication and curettage (EDC), surgical excision and Mohs micrographic surgery (MMS) at baseline, 12, 18 and 24 months.\textsuperscript{15} The study had a significantly larger sample size than previous studies and a longer follow up. Chren and colleagues used the dermatology-specific Skindex-16 score\textsuperscript{3} to measure QOL through subscales that cover symptoms, emotions and functioning. Skindex-16 scores range from 0–100, where higher scores correspond to a poorer QOL. The Skindex-16 scores of NMSC patients were relatively low in all treatment groups, indicating a higher QOL than in patients with psoriasis, atopic dermatitis or acne vulgaris. Improvements in QOL were statistically significant in patients who underwent MMS surgery in all subscales ($P \leq 0.001$) and excision (symptoms and emotions: $P \leq 0.001$, functioning: $P \leq 0.05$) but not in those who underwent EDC.\textsuperscript{15} While the Skindex-16 was able to detect differences in QOL between surgical interventions, overall scores remained low compared to other pathologies, suggesting that a more specific instrument may be necessary to fully capture the impact on QOL imposed by NMSC.

Chen and colleagues\textsuperscript{16} set out to determine the predictors of post-treatment QOL in the same set of NMSC patients. The group used the 12-item short form health survey (SF-12), composed of physical and mental health components, in addition to the Skindex-16 values. Patients with small tumours or with a tumour that was not within the cervicofacial region presented with better pretreatment QOL. No tumour or demographic characteristic independently predicted post-treatment QOL. Pretreatment QOL was the strongest predictor for post-treatment skin-related QOL, followed by better mental health status and fewer comorbidities. Although these findings are not unique to NMSC,\textsuperscript{25,24} they suggest that the Skindex-16 may lack the sensitivity needed to capture the decrement in QOL caused by NMSC.

In 2003 Rhee and colleagues\textsuperscript{2} investigated QOL in 121 patients with high-risk cervicofacial NMSC using generic QOL instruments in a longitudinal study.\textsuperscript{2} The patients completed the SF-56 and the functional assessment of cancer therapy-general (FACT-G) at baseline, 1 month and 4 months post-treatment. Their SF-56 scores were comparable to the normal population and the FACT-G values were high, indicating better QOL than in other malignancies. While there was no significant relationship between the SF-56 and the size, location and extent of the NMSC, the involvement of a functional area significantly correlated with the pain subscale. At 1 and 4 months’ post-treatment Rhee et al.\textsuperscript{22} found that the mental (SF-56) and the emotional (FACT-G) subscales significantly improved post-treatment. Interestingly, the FACT-G emotional well-being subscale significantly improved post-treatment, particularly in patients who were younger than 65 years and employed, suggesting the lesion was of greater importance. A 10-cm visual analogue scale revealed that at 4 months after surgery this same age group found the scar less bothersome than the lesion itself, whereas the reverse was true initially at 1 month. Rhee’s group recognised that NMSC patients were unique in the fact that the cancer was potentially less grave than other malignancies yet it most commonly involved an area of the body that is more conspicuous. Overall QOL of life scores proved to be similar to those expected in the normal population. The authors attributed the results to the insensitivity of the instruments they selected and recognised the need for a disease-specific instrument.

Using the same set of NMSC patients, the authors proceeded to determine whether there was a change in QOL pretreatment and post-treatment using the DLQI.\textsuperscript{17} The DLQI yielded a decrease in the subscale on pain, pruritus and soreness ($P = 0.005$), as well as a decrease in the influence of the skin on the patients’ choice of clothing post-treatment ($P = 0.001$). Similar to the study by Blackford and colleagues, the overall QOL scores revealed little handicap at the initial visit and showed little change post-treatment. These results led the authors to conclude that a more disease-specific health status instrument may be necessary to capture the effect of NMSC on QOL.\textsuperscript{17}

Shah and Coates\textsuperscript{26} sought to assess the QOL in elderly patients with skin disease. Using the DLQI, the hospital anxiety and depression scale (HADS)\textsuperscript{25} and the illness perception questionnaire (IPQ),\textsuperscript{26} Shah and Coates evaluated 100 patients with a variety of skin pathologies classified as either a lesion or a rash. There were 45 patients with a rash and of the 55 patients with cutaneous lesions, 21 had BCC, two had squamous cell carcinoma (SCC) and 11 had actinic keratoses (AK). Patients with rashes scored significantly higher on the HADS total score, DLQI score and the IPQ time and consequences subscales, corresponding to a significantly lower QOL than in patients with lesions. The IPQ controllability/cure subscale showed no difference between the rash and lesion groups. Patients with BCC reported a mean DLQI score of 2%, demonstrating little reduction in their QOL.\textsuperscript{18} The DLQI results in BCC patients were similar to those reported by Blackford and colleagues (mean DLQI score: 5%)\textsuperscript{25} and Rhee and colleagues (mean DLQI score: 2%).\textsuperscript{15} The DLQI results for patients with SCC and AK were not reported. The individual HADS and IPQ scores for BCC, SCC and AK patients were also not reported. The results of the study indicated that, compared to some other dermatological pathologies, NMSC exerts a less significant burden on QOL, however the study was limited by the small number of patients with NMSC and the disparity in duration between the lesions and rashes cohorts.
Rhee’s group was the first to recognise the need for a comprehensive disease-specific instrument to adequately capture the impact of NMSC on QOL and the authors proceeded to develop the skin cancer index (SCI). To construct the tool, four doctors (a dermatologist, facial plastic surgeon, oculoplastic surgeon, plastic surgeon), two nurses and a group of 20 patients who had undergone treatment for cervicofacial NMSC in the previous year were recruited. Through a process of item generation and refinement, a 15-item questionnaire was constructed with three subscales; emotional (seven items), social (five items) and appearance (three items).

Rhee’s group utilised the SCI in combination with the DLQI in a study of 185 cervicofacial NMSC patients assessed at baseline and at 4 months post-treatment. The SCI scores demonstrated that patients who were women, <50 years old and in employment experienced a greater impact on their QOL. Cancers located on the lip also had a greater impact on individuals’ QOL. Younger patients, patients who had no previous NMSC and the female sex predicted greater improvements after treatment in QOL over time. These associations were perhaps due to its effects on cosmesis and functional considerations. Generally, patients with a tumour on a highly visible facial site perceived the area post-treatment as less attractive. The concern for facial scarring on a highly visible facial site perceived the area post-treatment as less attractive. The concern for facial scarring on a highly visible facial site perceived the area post-treatment as less attractive. The concern for facial scarring on a highly visible facial site perceived the area post-treatment as less attractive. The concern for facial scarring on a highly visible facial site perceived the area post-treatment as less attractive.

In a recent systematic review of QOL instruments used in NMSC, the SCI was acknowledged as the only disease-specific health status instrument that had been developed and validated in this setting. The Skindex and DLQI scales were also discussed and were found to be limited in their ability to capture the disease-specific effects of NMSC. The SCI was thought to be superior to other QOL instruments with its comprehensive though focused emotional, social and appearance subscales. Among other dermatological health status instruments, the SCI is unique in its appearance subscale. The authors recognised the advantages of evaluating the perception of appearance pretreatment and post-treatment with questions addressing scarring, scar dimensions and effects on attractiveness. The authors proposed that because of its comprehensibility and specificity, the SCI proved to be the most useful health status instrument in NMSC patients. However, this study focused solely on QOL instruments and did not address the evolving role of utilities in this setting. One of the significant handicaps of the SCI is that by virtue of being a disease-specific instrument it cannot be used to compare the impact on QOL across a broad spectrum of pathologies. Utility weightings need to be considered as a potential method of quantifying QOL on a larger scale to facilitate comparisons between different health states across medicine.

**QUALITY OF LIFE UTILITY WEIGHTINGS**

In the setting of QOL, a utility represents a cardinal measure of the preference for a specific health status or outcome. Traditionally, methods such as the time trade-off (TTO), standard gamble or willingness to pay (WTP) are used to generate a utility weighting. The TTO method may involve asking patients how much time in terms of years, months and days they would give up to never have had a particular pathology or experienced the treatment for that pathology. The standard gamble usually involves giving patients a choice to assume a risk of immediate death for immediate cure, employing an algorithm based on the preferences reported to determine a utility weighting. WTP is a measure of disease burden that may be acquired directly from the patient by asking what fraction of income or amount they would be willing to pay to rid themselves of their current health condition. Utility weightings are assigned to different health states ranging from 1, representing perfect health, to 0, representing death. As utilities reflect a preference for a specific health outcome and are applicable to a broad range of conditions, utilities have become considered by health economists as the most appropriate metric to integrate QOL into cost-effectiveness analyses. Additionally, policy-makers use utilities as proxy for burden of disease to guide health-care and research fund allocation and, accordingly, utilities are emerging as an important parameter in health care and a number of utility weightings have been derived for NMSC (Table 2).

Chen and colleagues identified the importance of utilities and their role in assessing QOL in dermatology in 2004. The group sought to obtain utility weightings for various dermatoses using the TTO method in order to compare the relative burden of disease. The study yielded a mean utility value of 0.976 for NMSC, corresponding to a minimal impact on QOL. Unfortunately, patients with BCC and SCC were combined in a NMSC group and no information on the stage of disease was reported. Additionally, the patients’ individual and tumour characteristics specifically for NMSC were also not reported. The power of this study was limited due to the small number of patients with NMSC and the lack of information regarding the stage of disease. Nevertheless, this study established preliminary results and the need for further investigation using utilities in dermatology.

In 2008 a study by Lear and colleagues attempted to directly assess QOL in 41 NMSC patients using the standard gamble method. Patients referred to a tertiary skin cancer clinic with a cervicofacial NMSC were presented with two standard gamble scenarios; the first involving a BCC on the nose and the second a SCC on the lip. No patient was willing to assume more than a 1 in 100 risk of death to cure the condition presented in either scenario. Accordingly the utility weighting generated was 0.99 for NMSC, suggesting a minimal impact on patients’ QOL. The results were unsurprising, given that gamble scenarios involving a risk...
of death in a condition perceived as non-fatal are unlikely to yield valid results. In addition, the results indicated deficits in the patient’s understanding of the nature of NMSC, given there was no preference observed for BCC over SCC (with its increased metastatic potential). The authors reported that many patients expressed concerns regarding the treatment with regards to wait times, scarring and possible complications; however those concerns were not reflected in the QOL scores obtained from the scenarios.

An American study led by Seidler and colleagues33 sought to evaluate the cost-effectiveness of traditional excision versus MMS using quality-adjusted life-years as the measure of effectiveness. The authors generated a utility weighting using the TTO method in 98 patients, using two hypothetical health states; simple closure (secondary intention or primary closure) and complex closure (flap or graft). The TTO method involved asking the patients two questions: ‘How much time in terms of years, months, and days would you give up to never have had the (simple or complex) scar from your cancer surgery?’ and ‘How much time would you give up to never have had NMSC or the experience of going through the surgery for your facial NMSC?’.

The mean utility for any surgical excision was 0.996 (0.984–1) corresponding to 1 month of life traded. The mean utilities reported were 0.984 (0.974–1) for simple closure and 0.974 (0.953–1) for complex closure with recurrence, associated with a utility value of 0.984 (0.949–1) representing 3 months.

Seidler and colleagues31 subsequently sought to investigate QOL using the WTP technique in 87 patients with a range of dermatological conditions. The study included five patients with a BCC and seven patients with AK. The patients were asked how much they would be willing to pay for two theoretical drugs, one to control and another to cure their condition. These amounts were then calculated as a fraction of their annual income. The patients also completed the Skindex-29 and a TTO survey. Having BCC had the smallest impact on QOL when measured by the Skindex-29; however the TTO and WTP utility weightings showed a more moderate impairment. Patients with BCC yielded a utility value of 0.95 (0.88, 1.00) and were willing to pay 5% (1.40, 8.40) of their income for a control drug versus a one-time 1% (0.97, 16.53) of their income for a cure. Patients with AK had a comparatively high WTP for a cure (11% (5.71, 24.00) of income). However, most were reluctant to pay for a control drug (0.6% [0.21, 2.67] of annual income). Patients with AK yielded a TTO utility value of 1.00 (0.85, 1.00), demonstrating that AK has ostensibly a negligible impact on QOL. This study was limited by the very small number of patients with specific dermatological conditions. Additionally, the higher WTP for a control drug versus a one-time cure in BCC patients may indicate that the patients were confused by the survey. Furthermore, the effect of patients’ characteristics on WTP was not thoroughly investigated. Nevertheless, Seidler and colleagues’ study gave a good snapshot of the use of utilities to investigate the burden of skin diseases and stimulates further implementation in dermatology.

More recently, Shingler and colleagues34 conducted a sponsored study to help derive TTO utility weightings for advanced BCC (aBCC), defined as BCC that has progressed to become life-threatening, unresectable, locally advanced or metastatic.35 The study involved the construction of nine health states associated with aBCC through interviews with two dermatologists. A sample of 100 members of the general public were recruited and asked to rate the health states on a 0–100 point scale, where 0 represented death and 100 was full health. The participants were also asked to choose

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<td>Lear et al.32</td>
<td>NMSC patients (n = 41)</td>
<td>BCC</td>
<td>0.999 ± 0.005 SD</td>
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<td>A gamble scenario involving a risk of death with a condition perceived as non-fatal is unlikely to yield valid results.</td>
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<tr>
<td>Seidler et al.35</td>
<td>NMSC patients (n = 98)</td>
<td>Excision</td>
<td>0.996 (95% CI: 0.984–1.00)</td>
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<td>Time trade-off completed on patients who experience surgical management of NMSC</td>
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<td>Chen et al.4</td>
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<td>NMSC</td>
<td>0.976 ± 0.052 SD</td>
<td></td>
<td>BCC and SCC were combined in a NMSC group and no information on stage of disease was reported.</td>
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<tr>
<td>Seidler et al.33</td>
<td>NMSC patients (n = 12)</td>
<td>BCC</td>
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<td></td>
<td>Mixed results suggest patients may not have understood or completed study correctly</td>
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<td>Shingler et al.34</td>
<td>General public (n = 100)</td>
<td>aBCC with complete response:</td>
<td>0.94 (95% CI: 0.92–0.95)</td>
<td></td>
<td>Study limited by the accuracy of vignettes, the small number of scenarios and lack of patient involvement in initial construction of vignettes.</td>
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For the table above:

- **Study** - The study conducted
- **Patients** - The number of patients in the study
- **Health status** - The health status described in the study
- **Utility weighting** - The utility weighting reported
- **Error** - The error range for the utility weighting
- **Comment** - A comment about the study or the utility weighting reported

aBCC, advanced basal cell carcinoma; AK, actinic keratoses; IQR, interquartile range; NMSC, non-melanoma skin cancer; SCC, squamous cell carcinoma.
between living in the health state depicted by the vignette for 10 years or in a state of full health for a 10-\text{y} years. Utility weightings generated ranged between 0.67 (vignette: progressive disease with growth of 6 cm) and 0.94 (vignette: complete response to treatment). These utility weightings were considerably lower than those reported by Seidler and colleagues\textsuperscript{31,33} and Chen and colleagues,\textsuperscript{4} suggesting a more significant QOL burden was associated with aBCC. Multiple small lesions were seen as less preferable to a single small lesion, and similarly larger lesions were less preferable to the equivalent state with a smaller lesion. The post-surgical state received a relatively lower rating when compared to full health, perhaps indicating the perceived burden associated with extensive surgical intervention. The study was limited by the accuracy of the vignettes themselves, the constrained number of scenarios and lack of patients’ involvement in the initial construction of vignettes. Shingler and colleagues’s study suggests that an aBCC exerts an appreciable impact on individuals’ QOL and reinforces the potential of utilities in the context of NMSC.

CONCLUSION
NMSC exerts a small but appreciable impact on QOL.\textsuperscript{56} The literature to date has identified an appreciable health burden using both QOL instruments and studies generating utility weightings ranging from 0.67 to 1.00. Quantifying the burden on QOL is encumbered by the relatively minor nature of the insult posed, which influences the precision and validity of the results obtained. The SCI represents a promising, disease-specific, patient-based measure and should be considered as a valuable outcome measure for future research in NMSC. Further work is also warranted in the domain of utility weightings, as this is becoming an increasingly important means of comparing health states across medicine and is of particular importance from a health-care policy perspective, as it is considered in resource allocation. To date, research has centred on the burden imposed by discrete NMSC lesions. However, no one has considered evaluating NMSC as a chronic health condition. In Australia we frequently encounter the so-called actinopath (patients which widespread actinic damage, which is often managed as a chronic health state with serial monitoring and management) and an evaluation of the QOL of these patients represents another avenue for further investigation. The small but definite impact on their QOL posed by NMSC should be recognised by clinicians and warrants further evaluation by researchers in this field.

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REFERENCES


