

## Quality of life issues faced by patients with keratinocyte cancer: A systematic review

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### ARTICLE INFO

#### Keywords:

Keratinocyte cancer  
Skin neoplasms  
Basal cell carcinoma  
Cutaneous squamous cell carcinoma  
Quality of life

### ABSTRACT

**Introduction:** Keratinocyte carcinomas (KC), including basal cell carcinoma (BCC) and cutaneous squamous cell carcinoma (cSCC), represent the most prevalent malignancy worldwide with a rapidly increasing incidence. While KC and its treatment can negatively impact patients quality of life (QoL), existing QoL instruments lack specificity for unique KC-related issues. This systematic review explores the relevant QoL issues pertinent to patients with KC.

**Methods:** Literature from Ovid MEDLINE, Embase, and Cochrane Central Register of Controlled Trials databases from 1946 to January 2023 was systematically reviewed. Two independent reviewers screened and extracted studies of all designs discussing KC-specific QoL issues.

**Results:** The systematic review identified prevalent QoL issues in the literature. Some generic QoL-related issues are covered by more general cancer QoL instruments that are not site specific to KC, such as the EORTC QLQ-C30. These include pain, functioning, daily activities, work, leisure time, and social and family relationships. More KC-specific issues include the impact of cosmetic outcomes on QoL, such as scarring, skin pigmentation change, embarrassment, distress, and social withdrawal. Improved sun awareness, including increased sunscreen use, avoidance of outdoor activities, and sun-protective clothing usage, emerged as common changes in behavior. These issues may result from both the disease and the treatment.

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*Conclusions:* This review has identified multiple KC-specific QoL issues, highlighting need for a tailored QoL instrument to measure these KC-specific issues. As the landscape of KC research and treatment modalities evolve, a gap persists in terms of a standardized QoL measurement for both clinical and research contexts. A new QoL instrument needs to be developed which is better tailored to the needs of patients with KC.

## 1. Introduction

Non-melanoma skin cancers (NMSC) are comprised of basal cell carcinoma (BCC), cutaneous squamous cell carcinoma (cSCC), and a host of other rare tumors. BCC and cSCC are collectively referred to as keratinocyte carcinomas (KC). Amongst all cancers, KC is the most prevalent malignancy with a rapidly increasing incidence, largely due to the aging population [1]. Annually, 5.4 million KC cases are diagnosed in the US [2]; in Australia, 69% of residents are estimated to undergo at least one excision for KC in their lifetime [3].

Quality of life (QoL) in patients with KC can be influenced by various factors including the tumor itself, treatment modality, symptoms, functional limitations, cosmetic burden, and auxiliary considerations such as cost and disruption of activities of daily living [4,5]. It is important to note that the majority of these patients are diagnosed with low-risk disease and are less likely to experience severe symptoms. However, even mild or moderate complaints can have a disproportionately large impact on QoL, especially their perceived well being [4,5]. Five percent of patients with KC present with an advanced stage or are considered at “high risk” (e.g. cSCC T2/T3 UICC 8th Ed. or T2b/T3 by Brigham and Women’s Hospital (BWH) classification) of loco-regional recurrence (LRR) [6]. These high-risk cases, specifically cSCCs, can be challenging to manage, potentially resulting in metastases, mortality, and further deterioration of QoL. The treatment for LRR or distant metastases often involves radical, invasive interventions having substantial morbidity with limited efficacy [7].

Both the disease and therapeutic interventions, including surgical resection, radiation therapy, systemic treatment, or their combinations can adversely impact the QoL of patients with KC, particularly in functional and psychosocial domains [8]. KC commonly occur in the head and neck region, resulting in cosmetic changes that can lead to dissatisfaction with appearance and impaired self-esteem, disruption of social relationships, and ultimately social withdrawal. Functional changes may cause difficulties with oral intake, impaired visual and hearing capacity, and decreased communication ability. For extremity locations, digit or limb amputation may be necessary, resulting in significant functional impairment. Furthermore, anxiety surrounding the diagnosis, fear of recurrence or future KC diagnoses are common psychological burdens and detrimental contributors to QoL [9]. In addition, international guidelines and oncology societies, such as the European Society for Medical Oncology and American Society of Clinical Oncology, highlight the importance of investigating acute and long-term toxicities of oncologic therapies and QoL of cancer survivors [10,11].

In light of the above, we conducted a systematic review to explore the relevant QoL issues pertinent to patients with KC. This systematic review is the first step in the EORTC phase 1 project aimed at determining whether there is a necessity for a new QoL questionnaire specifically for KC. The project focuses on (1) identifying domains and issues discussed in the literature that are important to patients diagnosed with KC, (2) determining current QoL tools used in studies involving patients with KC, and (3) assessing the need for additional QoL item sets.

## 2. Methods

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [12].

### 2.1. Search strategy

A literature search was conducted reviewing all publications prior to February 1st, 2023, to identify records discussing QoL issues for patients with KC. Databases searched included Ovid MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials (CENTRAL). Keywords used were “skin neoplasm/cancer/carcinoma,” “quality of life,” “patient satisfaction,” and “patient experience/perspective”, among others (Appendix 1).

### 2.2. Article selection

Studies were included if they assessed QoL of adult patients with any type of KC. Reasons for exclusion were not assessing patients with KC independently from patients with other cancer sites, written in languages other than English, no extractable data (posters or abstracts), and study protocols. Records were screened via Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia (available at [www.covidence.org](http://www.covidence.org)) [13]. This is a collaborative web-based platform which organizes records and streamlines the production of systematic and other literature reviews by removing duplicates and allowing reviewers to screen studies independently [13]. Both title/abstract and full-text screening were completed independently by two reviewers (SKFK and SFL). The data of the included studies were extracted independently by two authors. Conflicts were resolved through discussion or by consulting a third author (EZ). Studies of any design assessing QoL issues for patients with KC were included.

### 2.3. Data collection and analysis

The following data were extracted: title, year of publication, assessment methods/questionnaires, study design, total participants, cancer site and all KC-specific QoL issues. Identified issues were extracted and sorted into the following six domains: physical, cosmetic, functional, psychological, social/behavioral, or issues with care.

## 3. Results

### 3.1. Study selection

The list of QoL issues was generated through a comprehensive systematic review of the literature (Fig. 1). The search identified 6093 records from Ovid MEDLINE, EMBASE, and CENTRAL. After duplicate removal, 4873 records were screened, of which 866 proceeded to full-text screening. Of these, 235 studies met selection criteria and were included for data extraction.

### 3.2. Study characteristics

The search identified 181 primary research studies (Table 1). The mean and median patient numbers were 183 and 50, respectively. Most studies were prospective, using surveys and questionnaires to quantify QoL issues (n = 113). There were also 25 retrospective studies. Two studies used mixed methods, and 41 employed qualitative methods. The qualitative studies also included 19 case reports and 14 case series.

Of the 181 studies, only 90 specified disease locations. The majority of papers focused on cancer sites such as the face or head and neck, and many investigated the nose. Fewer papers examined cervico-facial, eye, or back and shoulder sites. A smaller number of papers addressed the

genital/groin, lips, limbs, and scalp areas. Assessment tools used in the studies included Dermatology Life Quality Index (DLQI), the Skin Cancer Index (SCI), the Skindex scale, and the Visual Analogue Scale (VAS) (Table 2).

The remaining 54 records were non-primary studies (Table 3), including reviews, letters to editors, commentaries, guidelines, meta-analyses, and a learning activity. Meta-analyses, systematic reviews and structured reviews had a median of 23 papers included.

### 3.3. QoL issues

Extracted QoL issues were sorted into one of the six domains: physical, cosmetic, functional, psychological, social/behavioral, or issues with care (Tables 4 and 5).

### 3.4. Physical issues

Physical issues can arise from cancer or its treatment and include clinical signs, symptoms and outcomes or systemic reactions. Pain was the most common physical issue, with a study by Aymonier et al. (2022) revealing that post-surgical scarring-related pain impacted the daily lives of 28.6% of patients with BCC [14]. Other common complaints included itching, erythema, and ulceration. Dauden (2011) assessed Imiquimod 5% cream in 471 patients with superficial BCC, finding erythema as the most frequent side-effect, affecting 77.3% of patients, with 61.3% experiencing moderate to severe erythema [15]. Van

Winden et al. (2022) examined surgical complications, such as bleeding, infection, and sensory changes, in a cohort of 539 older adults with BCC, identifying tumor diameter was a significant predictor of treatment complications (OR, 1.07; 95% confidence interval (CI), 1.03–1.11;  $p = 0.001$ ) [16]. Studies reported on issues such as skin reactions, bleeding, infections, necrosis, and hair loss, as well as edema, nausea, and burning sensations. Symptoms such as nausea and diarrhea, muscle spasms/cramps, and weight loss often result from systemic therapies. Cavalieri et al. (2018) examined the QoL of 42 patients treated with dacomitinib for locally advanced or metastatic SCC, with patients experiencing diarrhea (71%), stomatitis (31%), nausea (12%), and vomiting (7%) [17]. These symptoms were reported less frequently in studies focusing on localized treatments.

Other studies highlight impediments related to systemic side effects from treatment. For instance, Davidson et al. (2002) reported 31.7% of NMSC patients sleeping more than usual, while Cavalieri et al. (2018) noted side effects, such as anorexia and dysgeusia among patients undergoing treatment with dacomitinib [17,18].

### 3.5. Cosmetic issues

Many studies focused on skin cancers in visible areas, such as the face, head and neck, and regions specifically around the nose or eyes. Consequently, cosmetic outcomes were frequently reported. Van Winden et al. (2022) found that being a female was predictive of lower cosmetic scores (effect size =  $-0.74$ ; 95% CI,  $-1.13$  to  $-0.30$ ;

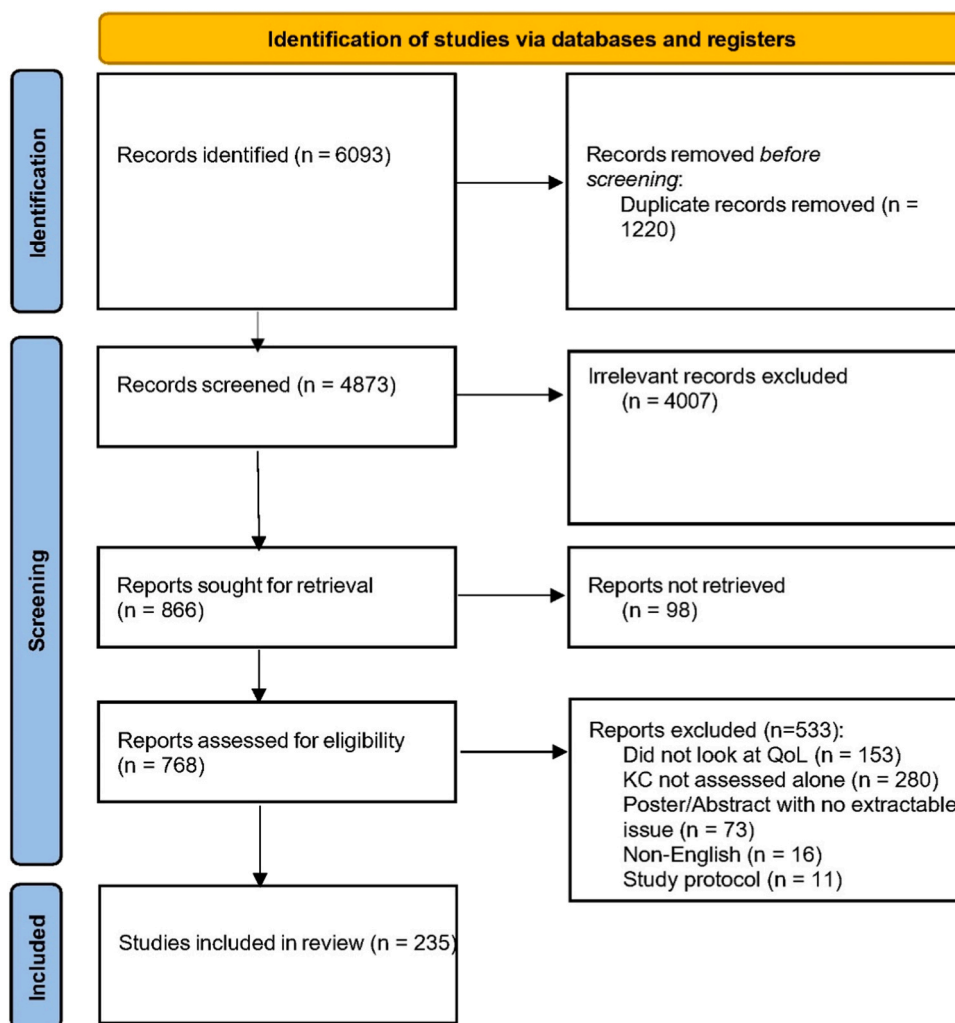


Fig. 1. PRISMA diagram.

**Table 1**  
Study designs of primary research studies (n = 181).

n	Prospective Quantitative Studies (n = 113)
42	<b>Unspecified</b> 7 abstracts only 1 thesis
26	<b>Clinical trials</b> 2 abstracts only 12 randomized control trials 2 sub studies
13	<b>Cohort studies</b> 1 abstract only
13	<b>Cross-sectional</b>
10	<b>Survey development or validation</b>
2	<b>Descriptive</b>
2	<b>Observational</b>
4	<b>Safety and efficacy evaluations</b>
1	<b>Case-control</b>
	<b>Retrospective Quantitative Studies (n = 25)</b>
19	<b>Retrospective chart reviews</b> 3 abstracts only
3	<b>Cohort studies</b>
3	<b>Other</b>
	<b>Qualitative or Mixed Method Studies (n = 43)</b>
19	<b>Case reports</b> 2 abstracts only
14	<b>Case Series</b> 1 also a review
8	<b>Qualitative</b> 2 abstracts only 1 also a review
2	<b>Mixed methods</b> 1 abstract only

p = 0.001) [16]. Additionally, several papers discussed scarring and changes in appearance. For example Sampogna et al. (2021) used the Skindex-29 to assess QoL differences between 364 women and men with KC, discovering that the mean score for worrying about scars was significantly higher among women than men (28.1 vs. 16.1,  $p < 0.001$ ) [19]. Scarring was reported in terms of visibility, noticeability, concern for scarring or disfigurement, and type of scarring, e.g. hypertrophic or atrophic. Aymonier et al. (2022) reported that 66.7% (158 of 237) of patients with BCC were bothered by esthetic problems or scarring caused by surgery [14]. Fewer papers discussed specific cosmetic changes, such as hypopigmentation and hyperpigmentation, which more commonly occur in patients treated with radiation or topical therapy, such as imiquimod 5% cream. Dauden et al. (2011) reported that 21.7% of patients developed hypopigmentation, while only 5.5% developed hyperpigmentation [15].

### 3.6. Functional issues

Fewer studies discussed functional limitations, with the most frequent being the impact on daily activities, effect on work, physical function, and general function. Impacts on daily activities included leisure activities, effect on sports, impacts on household work, and taking time off work. Steenrod et al. (2015) reported that 65% of the participants indicated that their skin condition negatively influenced their daily routines, affecting leisure activities, sports, household tasks, and even necessitating time away from work [20]. Aymonier et al. (2022) found that 28.6% (18 of 63) of patients with BCC reported having to miss work due to their cancer [14]. Abedini et al. (2018) reported the impact of NMSC on the QoL of 95 patients according to the DQLI and found a significantly higher impact on work or school for men than for women ( $p < 0.001$ ), and much greater if the tumor was in an exposed compared to a non-exposed location ( $p = 0.01$ ) [21]. Rhee et al. (2005) suggested patients felt their cancer impacted their ability to advance in their workplace. In their study that developed the new QoL instrument for NMSC, the Facial Skin Cancer Index, patients rated the effects of NMSC on their workplace advancement with a mean score of 3.33

**Table 2**  
Assessment Tools used in primary research studies involving patients with KC.

Number of Papers	Tool
15 +	Dermatology Life Quality Index Skin Cancer Index Skindex
5-14	Visual Analogue Scale Common Terminology Criteria for Adverse Events Eastern Cooperative Oncology Group Skin Assessment FACE-Q Functional Assessment of Cancer Therapy – General Hospital Anxiety and Depression Scale Radiation Therapy Oncology Group Skin Assessment Short Form Survey – 36, 20 or 12 Skin Cancer Quality of Life Impact Tool
< 5	Adapted melanoma questionnaire Anchor-based Questions Basal and Squamous Cell Carcinoma Quality of Life Berlin Questionnaire-Sleep apnea screening Brazilian Medical Outcomes Cancer worry scale Cranenburgh et al. Satisfaction scale Customized Perceived Stress Questionnaire Derriford Appearance Scale - 24 Dermatology Quality of Life Scales Epworth Sleepiness Scale European Medicines Agency EORTC QLQ-C30 EuroQol-5D-5 L Family Dermatology Life Quality Index Fatigue Severity Scale Functional Rhinoplasty Outcome Inventory 17 General Health Questionnaire Global Rating of Change Scale Groningen Frailty Index Importance of Appearance Scale Insomnia Severity Index International Atomic Energy Agency scale (Pain and Drug scores) International Restless Leg Scale Katz index Activities of Daily Living Lawton and Brody index of instrumental activities of daily living Lee index Leeds Sleep Evaluation Questionnaire Nasal Obstruction Symptom Evaluation Patient and Observer Scar Assessment Scale Patient Satisfaction Questionnaire – 18 Pittsburgh Sleep Quality Index Rand Corporation Health Survey RECIST system Rhinoplasty Outcome Evaluation Rosenberg Self-Esteem Scale Sickness Impact Profile Sport Anxiety Scale State-Trait Anxiety Inventory Sun-protective behaviors Supportive Care Needs Survey TELER scale Timed Up and Go Treatment Satisfaction Questionnaire for Medication Vancouver scale Ways of Coping Inventory - Cancer Version World Health Organization Wound-Quality of Life Survey

(standard deviation [SD] 1.46) on a scale of one to five, with five being most important [22]. Aymonier et al. (2022) revealed that 28.6% of patients with BCC had to skip work due to their ailment [14]. Similarly, Abedini et al. (2018) observed the NMSC's more significant interference in work or school for men, especially if tumors were on exposed locations [21]. Rhee et al. (2005) noted that patients felt their cancer impacted their potential for career advancement [22]. The effects on work also included financial aspects, which could be due to taking time off work or stress caused by poor insurance coverage. The question of health insurance coverage in the study by Rhee et al. (2005), had a high

**Table 3**  
Study designs of secondary research studies (n = 54).

Reviews (n = 40)	Reviews
31	1 also a data aggregate
6	Systematic reviews
3	Meta-analyses
	1 also a network meta-analysis
	1 also a systematic review
Other (n = 14)	Commentaries
3	1 abstract only
7	Letters to the Editor
3	Guidelines
1	Learning activity

mean score of 4.02 out of 5 (SD 1.43) [22], indicating that concerns about health insurance have a substantial impact on QoL.

Issues regarding general and physical function were also discussed in other studies using more specific terms, such as fatigue, feeling of listlessness, dysgeusia, sleep problems, difficulty with mobility, decreased/loss of appetite, ectropion/ptosis, and vision problems. Davidson et al. (2002), reported 31.7% of patients with NMSC were sleeping more than usual [18]. Cavalieri et al. (2018), reported that among patients being treated with dacomitinib 19% developed anorexia (grade 1 or 2) and 10% experienced dysgeusia [17].

### 3.7. Psychological issues

General emotional issues were the most frequently reported, followed by anxiety. Radiotis et al. (2014) surveyed 56 patients with either BCC or cSCC and found that 70% of patients reported feeling anxious about their skin cancer [23]. Long et al. (2022) studied preoperative anxiety levels among patients with NMSC. The study found that location was a significant predictor for perioperative anxiety, and surgery to the eyelid area caused the most anxiety (OR=14.0, p < 0.01) [24]. Sampogna et al. (2020) also found significant differences between the psychological QoL of men and women with KC. The overall Skindex-29 emotional subscale score was 14 for men and 18 for women (p = 0.012) [19]. Specifically, women scored significantly higher for depressive symptoms, with a score of 19.9, compared to a score of 13.4 among men (p = 0.013) [19]. Depression was discussed along with embarrassment, worry about cancer spreading, and concern about new skin cancers arising. Embarrassment often was linked to the noticeability of lesions or scars. Radiotis et al. (2014) identified a significant difference in embarrassment by age. Overall, 34% of patients reported embarrassment, but this figure increased to 62% in patients aged 60 or younger (p < 0.05) [23]. Similarly, worry was reported along with poor mental health, feeling self-conscious, and frustration.

Worry often concerned cancer and outcomes, such as worry about cancer evolution or the diagnosis negatively impacting mental health. Gerritsen et al. (2009), conducted a survey of 220 patients with BCC in the Netherlands and found that 52% of patients reported being frightened by the diagnosis of skin cancer but knew it was curable [25]. Burdon-Jones et al. (2009) found that 57% of patients reported feeling concerned that skin cancer could spread, recur, or develop [26]. Similarly, other specific worries included concerns about the future, the cause of skin cancer, potential family risk, and fear of cancer recurrence. Radiotis et al. (2014) reported that 77% of patients were worried about potential skin cancers in the future [23].

### 3.8. Social/behavioral issues and functioning

Issues with social function were discussed in general terms, while fewer studies examined the specific impact of KC on social matters. Abedini et al. (2018) identified significant differences in DLQI section

**Table 4**  
Frequency of QoL issues (physical, cosmetic and functional) identified in studies involving patients with KC.

Number of papers	Physical	Cosmetic	Functional
51+	• Pain	• Cosmetic outcome	None
31-50	• Itching	• Scarring	None
	• Erythema	• Appearance	
21-30	• Ulceration	None	• Daily activities
	• Skin reaction		• Effect on work
	• Bleeding		• Physical function
	• Infection		• General function
	• Necrosis		• Fatigue
	• Hair loss		• Financial concerns
16-20	• Edema	• Hypopigmentation	• Impacted leisure activities
	• Nausea	• Hyperpigmentation	• Issues with taste
	• Burning		• Sleep problems
11-15	• Wound dehiscence	• Telangiectasia	
	• Crusting	• Esthetic results	
	• Diarrhea	• Attractiveness	
	• Dermatitis	• Pigmentary alterations	
	• Muscle spasms/cramps	• Scar visibility	
	• Discomfort		
	• Weight loss		
	• Rash		
6-10	• Radiation toxicity	• Scar appearance	• Mobility
	• Reduced/lost sensation	• Skin-related quality of life	• Decreased/loss of appetite
	• Stinging	• Noticeable scar	• Effect on sports
	• Dry/peeling skin	• Concern for disfigurement	• Impacted household work
	• General health	• Concern for scarring	• Less energy
	• Atrophy	• Discoloration	• Ectropion/ptosis
	• Hematoma		• Vision problems
	• Erosion		
	• Soreness		
	• Bullous/blistering		
	• Graft rejection/failure		
	• Bodily pain		
	• Wound weeping/discharge		
	• Fibrosis		
	• Scaling		
	• Inflammation		
	• Moist desquamation		
	• Non/slow healing wound		
	• Constipation		
	• Flu-like symptoms		
	• Mucositis		
	• Vomiting		
	• Acne-like rash		
1-5	• Conjunctivitis	• Color match	• Functional limitations
	• Physical role	• Contour	• Breathing problems
	• Skin sensitivity	• Hypertrophic scarring	• Having to take time off work
	• Induration	• Asymmetry	• Watery eyes
	• Pneumonitis/pneumonia	• Dislike seeing yourself in mirror	• Impacted ability to eat
	• Abdominal pain	• Atrophic scarring	• Bathing/grooming
	• Headache	• Keloid	• Health insurance coverage
	• Mucocutaneous dryness	• Anorexia	• Nasal obstruction
	• Urinary tract infections		• Difficulty swallowing
	• Foul smell		• Dysphonia
	• Nerve damage		
	• Tenderness		
	• Corneal erosion		
	• Keratitis		
	• Restlessness in legs		

(continued on next page)

**Table 4** (continued)

Number of papers	Physical	Cosmetic	Functional
	<ul style="list-style-type: none"> <li>• Cranial nerve neuropathy</li> <li>• Joint pain</li> <li>• Nail changes</li> <li>• Physical well-being</li> <li>• Scabbing</li> <li>• Bump</li> <li>• Folliculitis</li> <li>• Arterial thrombosis</li> <li>• Contraction of the graft</li> <li>• Depressed grafted site</li> <li>• Wound breakdown</li> <li>• Poor tissue coordination</li> <li>• Cold intolerance</li> <li>• Gout</li> <li>• Overheating</li> <li>• Dyspnea</li> <li>• Facial palsy</li> <li>• Lymphedema</li> <li>• Malaise</li> <li>• Rhinorrhea</li> <li>• Tinnitus</li> </ul>		<ul style="list-style-type: none"> <li>• Changes in facial expressions</li> <li>• Functional well-being</li> <li>• Grip strength</li> <li>• Pinch power</li> <li>• Proptosis</li> <li>• Limited work advancement</li> <li>• Hearing loss</li> <li>• Decreased libido</li> </ul>

scores for personal relationships depending on gender and location of the tumor. They found that men were more likely to experience challenges in their personal relationships than women ( $p = 0.01$ ) [21]. The impacts on social relationships extended to intimate and sexual relationships, a need for support from friends and family, and concerns that the diagnosis may cause worry for friends and family. More specific challenges included the impact on social relationships or family life, as well as being bothered by questions or reactions from others, often about visible scarring. In the study by Burdon-Jones et al. (2009), 45% of patients reported feeling concerned about scarring or disfigurement and potential reactions from others [26]. These reactions could also correlate to not wanting to go out in public and feeling uncomfortable meeting new people. Radiotis et al. (2014) reported that 30% of patients said their cancer caused them to feel uncomfortable going out in public; among men, 44% were uncomfortable, which was significantly ( $p < 0.05$ ) higher than seen in women (19%). They also reported that 34% of patients felt uncomfortable meeting new people, but no significant differences were identified between genders [23].

Studies also discussed changes in sun safety habits and participating in fewer outdoor activities or staying out of the sun. Aymonier et al. (2022) reported that 92.8% (221 of 238) of patients with BCC changed their habits regarding sun exposure [14]. One of the studies by Rhee et al. (2004) looked more deeply at changes to sun-protective behaviors in patients with NMSC before surgery compared to four months post-operation. They found significant increases in sunscreen use (25.7%), wearing a hat or cap in the sun (21.8%), avoiding the sun between 10 AM and 2 PM (25.7%), and skipping sun-related activities (30.7%) ( $p = 0.001$ ) [27]. Increased sunscreen usage and covering skin from the sun were discussed.

### 3.9. Experience with care

While the primary focus of our review is on the QoL of patients with KC, we also observed a theme regarding patients' experiences and satisfaction related to the care they received. This distinction is important, as the nature of care and its associated logistics, while integral to the patient experience, might not directly affect QoL in the same way as clinical symptoms and psychosocial effects.

**Table 5**

Frequency of QoL issues (psychological, social/behavioral, or issues with care) identified in studies involving patients with KC.

Number of papers	Psychological	Social/ Behavioral	Issues with Care
31-50	<ul style="list-style-type: none"> <li>• Emotional</li> </ul>	None	None
21-30	<ul style="list-style-type: none"> <li>• Anxiety</li> </ul>	<ul style="list-style-type: none"> <li>• Social function</li> </ul>	<ul style="list-style-type: none"> <li>• Treatment satisfaction</li> </ul>
16-20	<ul style="list-style-type: none"> <li>• Depression</li> <li>• Embarrassed</li> <li>• Worried about new skin cancer</li> <li>• Concern about cancer spreading</li> </ul>	<ul style="list-style-type: none"> <li>• None</li> </ul>	<ul style="list-style-type: none"> <li>• None</li> </ul>
11-15	<ul style="list-style-type: none"> <li>• Mental health</li> <li>• Worry</li> <li>• Frustration</li> <li>• Self-conscious</li> <li>• Worried about cancer evolution</li> <li>• Diagnosis caused negative impact on mental health</li> </ul>	<ul style="list-style-type: none"> <li>• Change in sun safety habits</li> <li>• Impact in social relationships</li> <li>• Fewer outdoor activities/ staying out of sun</li> <li>• Bothered by questions/ reactions from others</li> <li>• Family life</li> <li>• Concern your cancer may worry your friends</li> <li>• Effect on love life</li> <li>• Need for family/ friends support</li> <li>• Increased sunscreen use</li> <li>• Impacted going out in public</li> <li>• Clothing limitations</li> <li>• Sexual relationship affected</li> <li>• Covering skin from sun</li> <li>• Checking skin</li> <li>• Uncomfortable meeting new people</li> <li>• Negative evolution of professional relations</li> <li>• Use of sun-protective clothing</li> <li>• General behavior</li> <li>• Altered diet</li> <li>• Harder to take care of family</li> <li>• Impact in emotional relationships</li> </ul>	<ul style="list-style-type: none"> <li>• Treatment convenience</li> <li>• Need for more information</li> </ul>
6-10	<ul style="list-style-type: none"> <li>• Cognitive functioning</li> <li>• Emotional role</li> <li>• Future concerns</li> <li>• Concern about the cause of skin cancer</li> <li>• Worry about family risk</li> <li>• Fear of cancer recurring</li> </ul>	<ul style="list-style-type: none"> <li>• Concern your cancer may worry your friends</li> <li>• Effect on love life</li> <li>• Need for family/ friends support</li> <li>• Increased sunscreen use</li> <li>• Impacted going out in public</li> <li>• Clothing limitations</li> <li>• Sexual relationship affected</li> <li>• Covering skin from sun</li> <li>• Checking skin</li> <li>• Uncomfortable meeting new people</li> <li>• Negative evolution of professional relations</li> <li>• Use of sun-protective clothing</li> <li>• General behavior</li> <li>• Altered diet</li> <li>• Harder to take care of family</li> <li>• Impact in emotional relationships</li> </ul>	<ul style="list-style-type: none"> <li>• Issues with treatment</li> <li>• Worry about treatment</li> <li>• Need to know more about prevention</li> <li>• Needed better HCP communication</li> <li>• Needed more support from hcps</li> <li>• Issues with wound care</li> <li>• Need for follow ups</li> <li>• Dissatisfied with care</li> <li>• Treatment accessibility</li> <li>• Need for a better patient-provider relationship</li> <li>• Unclear diagnosis</li> <li>• Need for shared decision making</li> <li>• Prefer to see a dermatologist for follow up</li> </ul>
1-5	<ul style="list-style-type: none"> <li>• General distress</li> <li>• relationship</li> <li>• Fear</li> <li>• Stress</li> <li>• Anger</li> <li>• Confusion</li> <li>• Guilt</li> <li>• Isolation</li> <li>• Loss of confidence</li> <li>• Weepy</li> <li>• Shame</li> <li>• Demanding</li> <li>• Disgust</li> <li>• Discouragement</li> <li>• Denial</li> <li>• Feeling less feminine/ masculine</li> <li>• Denial</li> <li>• Loneliness</li> <li>• Skin inconvenience</li> <li>• Tensed</li> <li>• Felt more aware of mortality</li> <li>• Worried about new different cancer</li> <li>• Fear of surgery</li> <li>• Fear of hospitals</li> </ul>	<ul style="list-style-type: none"> <li>• Concern your cancer may worry your friends</li> <li>• Effect on love life</li> <li>• Need for family/ friends support</li> <li>• Increased sunscreen use</li> <li>• Impacted going out in public</li> <li>• Clothing limitations</li> <li>• Sexual relationship affected</li> <li>• Covering skin from sun</li> <li>• Checking skin</li> <li>• Uncomfortable meeting new people</li> <li>• Negative evolution of professional relations</li> <li>• Use of sun-protective clothing</li> <li>• General behavior</li> <li>• Altered diet</li> <li>• Harder to take care of family</li> <li>• Impact in emotional relationships</li> </ul>	<ul style="list-style-type: none"> <li>• Issues with treatment</li> <li>• Worry about treatment</li> <li>• Need to know more about prevention</li> <li>• Needed better HCP communication</li> <li>• Needed more support from hcps</li> <li>• Issues with wound care</li> <li>• Need for follow ups</li> <li>• Dissatisfied with care</li> <li>• Treatment accessibility</li> <li>• Need for a better patient-provider relationship</li> <li>• Unclear diagnosis</li> <li>• Need for shared decision making</li> <li>• Prefer to see a dermatologist for follow up</li> </ul>

Satisfaction regarding treatment was investigated in several studies, while other topics were less frequently addressed. Lee et al. (2021) evaluated outcomes and treatment satisfaction for patients treated with Mohs micrographic surgery for NMSC using Patient Satisfaction Questionnaire-18, with a mean overall satisfaction of 4.35 out of 5. However, accessibility and convenience scored lower with an average of only 3.98 out of 5 [28], with comment on treatment convenience and the need for more patient information to be provided.

Furthermore, Ludgate et al. (2011) looked at internet use and found that out of 400 patients with NMSC, 63% of patients accessed the internet or used email for information about their condition in the 12 months before their diagnosis. They reported that 20% of participants with NMSC said they used the internet to verify information from healthcare professionals (HCPs) and 28% said that they found information that had not been provided by their HCPs [29].

It is worth mentioning that other studies touched on topics of patient concerns such as apprehensions about treatment, a desire for comprehensive information about skin cancer prevention, an expressed need for enhanced communication and support from HCPs, challenges related to wound care, and calls for improved post-treatment follow-up. For example, Burdon-Jones et al. (2010) highlighted that a substantial 71% of NMSC patients expressed concerns about the lack of recognition and understanding of skin cancer by general public [26].

#### 4. Discussion

This systematic review highlights several unique QoL issues for patients with KC. Patients with NMSC had greater “concern about the public’s lack of understanding and recognition of skin cancer” compared to patients with melanoma [26]. Most KCs occur on sun-exposed body parts such as the face, head, neck, and upper limbs [30], causing cosmetic concerns, especially among women [21,23]. Individuals with tumors in exposed locations were more likely to struggle in personal relationships [21]. Lower income, resulting in financial concerns, is also associated with worse overall QoL [31]. KC is predominantly diagnosed in older patients, who may face more challenges and have less access to online resources and support [29]. There were also interesting differences between genders, with women being more likely to experience psychological distress while men were more likely to experience struggles with their personal and professional relationships.

Early and low risk KCs are usually cured by surgery; however, patients may still experience shock and fear upon diagnosis. Effective communication about the disease and treatment success is crucial to reduce emotional distress. Treating high-risk KC or LRR can be challenging, particularly in those with comorbidities or poor performance status. Currently, there is no published patient decision aid for patients with high-risk BCC to decide between surgery and radiation, this decreases patient autonomy and creates more of a burden for clinicians [32]. Improved understanding of the QoL issues that may accompany these treatment options may help to further the development of decision aids and increase patient autonomy. However, when advanced KC, LRR, or distant metastases are not treatable with surgery or radiation therapy, targeted therapies such as vismodegib for BCC or cemiplimab for cSCC can be used. These agents are effective, but have the added risk of adverse effects, causing treatment disruption and potential worsening of QoL [33]. More recently immunotherapy with programmed death-1 (PD-1) immune checkpoint inhibitors has shown a therapeutic effect for advanced and metastatic cSCC [34]. Therefore, QoL questionnaires may be particularly helpful for patients by potentially assessing immune-related adverse events from their cancer treatment.

The systematic review highlighted the diverse range of QoL issues currently assessed in patients with KC, demonstrating that a no single assessment tool is comprehensive enough to encompass all relevant dimensions of QoL. While existing questionnaires, such as DLQI, SCI, Skindex, and VAS, offer valuable insights into certain aspects of QoL, they come with certain limitations. For instance, the VAS, commonly

used to measure pain, can also gauge mood, ambulation, appetite and more but is limited by its single-question format [35]. The SCI, DLQI, and Skindex, on the other hand, are more extensive, spanning multi-question surveys across various QoL domains. Lee et al. (2013) pointed out that since DQLI and Skindex were developed for all dermatological conditions, they may not capture NMSC-specific concerns [36]. Additionally, they do not assess the impact of scarring on QoL [37]. SCI covers appearance, emotional, and social domains but omits physical or functional symptoms and their impact on QoL [38]. Other tools also have limitations, such as validation only in surgical patients (SCI [39], BaSQoL [40]), inclusion of patients with melanoma (SCQoLIT [41]) or being specific to facial cancers (FACE-Q [42]). Given the vast array of issues presented by existing tools, there is need for a new instrument tailored to address KC-specific concerns more holistically.

#### 4.1. Strengths and limitations

A strength of this review is the inclusion of all studies on QoL of patients with KC without age or treatment restriction, enabling the assessment of relevant QoL issues for all patients with KC. Another strength is the substantial number of included studies, as well as qualitative studies and case reports. While many studies used validated tools to capture QoL data, this may lead to under-reporting of symptoms because they are not individually recognized and assessed. Considering a diverse range of studies allows our review to provide a comprehensive overview of the various issues currently assessed, but it does not pinpoint those that may be overlooked by existing instruments and therefore may be areas of unmet need. For instance, existing questionnaires may fail to capture issues of importance to these patients. Another limitation is the inclusion of secondary research studies, which may have assessed primary research studies already evaluated in this review, leading to possible duplication of discussed issues and may make some issues appear more prevalent.

#### 5. Conclusion

These results underscore the unique QoL issues faced by patients with KC, emphasizing the need for a comprehensive QoL tool tailored to this population. As research and treatment options (e.g., immunotherapy, targeted therapy) for KC continue to expand, there is an unmet need for a standardized KC QoL assessment tool in both clinical practice and research studies. This review demonstrates that many QoL concerns are present among patients with KC which are not captured in existing assessment tools. There is a clear need for the development and subsequent testing of a new QoL assessment that is sensitive and specific to the experiences of patients with KC. The development of such a questionnaire should focus on validating these issues and in order to meet guideline recommendations for assessing the acute and long-term toxicities of oncologic therapies and the QoL of patients with KC.

#### Funding

This research was funded by the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Group (QLG), grant number 007-2023. The EORTC QLG business model involves license fees for commercial use of their instruments. Academic use of EORTC instruments is free of charge.

#### CRediT authorship contribution statement

**Vassiliou Vassilios:** Writing – review & editing, Supervision, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization. **Bonomo Pierluigi:** Writing – review & editing, Supervision, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization. **Chan Adrian Wai:** Writing – review &

editing, Methodology, Investigation, Formal analysis. **Mir Romaana:** Writing – review & editing. **Wong Henry CY:** Writing – original draft, Methodology, Investigation, Formal analysis. **Hirakawa Satoshi:** Writing – review & editing. **Sodergren Samantha:** Writing – review & editing. **Chichel Adam:** Writing – review & editing. **Oren Dana:** Writing – review & editing. **Kouloulis Vassilis:** Writing – review & editing. **Egeler Mees:** Writing – review & editing. **Chow Edward:** Writing – review & editing, Supervision, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization. **Oldenburger Eva:** Writing – review & editing, Formal analysis. **Rembielak Agata:** Writing – review & editing, Supervision, Investigation, Funding acquisition, Formal analysis, Conceptualization. **Young Teresa:** Writing – review & editing. **Kennedy Samantha K.F.:** Writing – original draft, Project administration, Investigation, Formal analysis, Data curation. **Chalk Tara:** Writing – review & editing. **Lee Shing-Fung:** Writing – review & editing, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Alchek Yifat:** Writing – review & editing. **Zhang Elwyn:** Writing – original draft, Formal analysis, Data curation. **Barnes Elizabeth A:** Writing – review & editing, Supervision, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization. **Gojsevic Milena:** Writing – original draft, Formal analysis, Data curation. **Rajeswaran Thenugaa:** Writing – original draft, Formal analysis, Data curation.

### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.ejcskn.2024.100022](https://doi.org/10.1016/j.ejcskn.2024.100022).

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