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ORIGINAL RESEARCH

# A Qualitative Comparison of Symptoms and Impact of Varying Stages of Basal Cell Carcinoma

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## ABSTRACT

***Introduction***: Basal cell carcinoma (BCC) is the most common form of skin cancer; however, few data are available relating to patients' perspectives and experiences of this disease. This study explored the spectrum of BCC symptoms and their impact by disease stage to determine how BCC affects the overall health-related quality of life (HRQL) of patients.

***Methods***: This study comprised a cross-sectional, qualitative approach involving telephone interviews with patients with BCC who had been divided into two groups: group 1 (G1), patients with stage 1, non-advanced BCC (and of superficial or nodular histology); and group 2 (G2), patients with locally advanced or metastatic BCC. Patients were recruited from three clinical sites in the USA based on a separate qualitative interview study (I4J-MC-HHBB [1.3]) over a 10-month period. Techniques in qualitative methodology were used by applying 'open-ended' questions and probing techniques intended to elicit patients' own description of their experiences with BCC. Telephone interviews lasted between 60 and 90 mins.

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***Results***: Thirty-four interviews were conducted (G1: $N = 13$; G2: $N = 21$). The majority of patients were aged either 55–64 years (32%, $N = 11$) or 76+ years (32%, $N = 11$) and were primarily male (82%, $N = 28$); most (75%, $N = 24$) patients were actively receiving BCC treatment. Both groups reported similar symptoms, with the most common being red lesions or open sores that failed to heal (41%, $N = 14$) and cancer-related stress (41%, $N = 14$). G2 reported more frequent and severe HRQL impact as a result of their cancer condition because most were affected in their daily activities (76%, $N = 16$) or emotional well-being (71%, $N = 15$). Cosmetic and functional impacts were relevant and important aspects of HRQL for both patient groups (G1: 31%, $N = 4$; G2: 48%, $N = 10$).

***Conclusions***: Patients with non-advanced or locally advanced and metastatic BCC experience disease-related symptoms that affect their HRQL, activities of daily living, emotional well-being, and social and/or leisure activities. Qualitative descriptions of patient experiences can help healthcare providers and caregivers better understand the impact of BCC from the patient perspective.

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**Keywords:** Basal cell carcinoma (BCC); Dermatology; Health-related quality of life (HRQL); Locally advanced; Metastatic; Non-advanced BCC; Non-melanoma skin cancer (NMSC); Qualitative; Symptomatology

## INTRODUCTION

Basal cell carcinoma (BCC) is the most common cancer among fair-skinned individuals, with a wide range in age-standardized annual incidence by country from approximately 44–745 per 100,000 for women and 54–1041 per 100,000 for men in Germany and Australia, respectively [1–3]. The incidence of non-melanoma skin cancer (NMSC), and specifically BCC, is increasing worldwide. The incidence of NMSC procedures in the USA has almost doubled since 1994, and the total number of new cases in 2006 was estimated at 3.5 million per year, approximately 80% of which were BCC [4]. By 2030, it is anticipated that the number of cases presenting to dermatologists could increase by an estimated 50% [5]. Given that primary BCCs occur mostly on the areas of the body with the greatest sun exposure, approximately 70% occur on the head or face [6]. Less than 5% of all BCC cases become locally advanced or metastatic [7]. However, if untreated, these lesions can cause substantial local tissue destruction and disfigurement [8]. Most BCC lesions can be removed through surgical measures; however, a small percentage of patients are unsuitable for surgery (because of the location or size of the lesion) or develop a more advanced stage of disease. These patients constitute a poorly defined (but small) percentage of overall BCC [9] and might have a greater disease impact [10].

Although several efforts have been made to determine the impact of NMSCs on the health-related quality of life (HRQL) of patients [11–14], few studies have examined the specific impact of BCC. Patient-reported outcome (PRO) measures, such as the Skindex, Dermatology Life Quality Index (DLQI), and Short-form Health Survey-12 (SF-12), have been administered in studies of NMSC; however, these measures were designed to evaluate more general aspects of HRQL for non-cancer skin conditions [13, 15, 16]. Rhee et al. [17] developed and validated the Skin Cancer Index (SCI) to address the need for a disease-specific HRQL instrument in NMSC;

however, their study population was not BCC specific and only focused on patients who experienced skin cancer in the cervicofacial region. Burdon-Jones et al. [18] recognized and attempted to address the lack of knowledge related to non-metastatic skin cancer PRO measures by eliciting general opinions in writing from patients with malignant melanoma and NMSC, and concluded that a disease-specific measure for patients with both metastatic and non-metastatic disease was needed. Shingler et al. [10] conducted a health utility study that found that severe forms of BCC can represent a significant psychological and cosmetic burden to patients, but these results were quantitative and did not give patients the opportunity to describe the burden in their own words. A recent study by Mathias et al. [19], undertaken to develop a BCC-specific PRO measure, found more substantial impacts related to daily activities and psychosocial effects in patients with more advanced stages of disease (locally advanced, metastatic BCC) compared with patients with basal cell nevus syndrome. However, consistent with Shingler et al. [10], Mathias et al. [19] did not provide an in-depth qualitative understanding of the patients' perspectives.

Given that little has been done to fully understand experiences of BCC directly from patients, the primary objective of this study was to better characterize symptoms, the bothersomeness of symptoms, and the HRQL impact of BCC on the daily lives of patients across different stages of the disease. A secondary objective was to compare descriptively the experiences, symptoms, and HRQL impact of patients with non-advanced (including only superficial or nodular histology) BCC with those of patients with locally advanced or metastatic disease.

# METHODS

## Study Design

This was a cross-sectional, qualitative study involving 34 telephone interviews with patients with BCC. Patients were recruited into two study groups depending on their disease stage using the American Joint Committee on Cancer (7th edn) staging criteria [20]: group 1 (G1) included patients with stage 1, non-advanced, BCC and group 2 (G2) included patients with locally advanced or metastatic BCC. Most patients ($N = 32$) were recruited from three clinical sites in the USA (two in California and one in Michigan). Two patients with BCC were recruited as part of a qualitative interview study (I4J-MC-HHBB [1.3]) that was being run in parallel to an ongoing, phase I, dose-escalation study (ClinicalTrials.gov #NCT01226485) for patients with advanced cancer (including a locally advanced or metastatic BCC group). All patient recruitment took place over the course of 10 months (March 2013–December 2013). This parallel interview study was terminated early because of a lack of enrollment, but the data from the two interviews were included in the current analysis.

Institutional review board (IRB) approval was obtained before the start of the study and all procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964, as revised in 2013, and Good Clinical Practices. All patients provided written informed consent before the start of the interview.

### Patient Recruitment

Patients were identified from patient databases or medical records at each clinical site or through participation in the ongoing clinical trial (ClinicalTrials.gov #NCT01226485). All patients were required to be aged 18 years or older, be able to participate in a telephone interview in English, and have the presence of measurable disease at the time of screening as defined by the Response Evaluation Criteria in Solid Tumors (RECIST 1.1). All patients had active disease that was either newly diagnosed or recurrent; G1 had been diagnosed with non-advanced BCC (including only superficial or nodular histology) and all patients in G2 had a diagnosis of BCC that was locally advanced or metastatic [20]. There were no restrictions based on location of the patients' lesion(s) for participation in the study. Patients were not eligible if they had a clinically relevant medical or psychiatric condition that, in the opinion of the investigator or site coordinator, would interfere with the patient's ability to complete the study.

### Data Collection

All patients were screened over the telephone by site coordinators for inclusion in the study. Informed consent forms were mailed to patients and reviewed with scientific staff over the telephone before the start of the interview. Verbal and written informed consent was obtained from each patient. Patients participated in one telephone interview lasting between 60 and 90 min. All scientific staff was trained in the appropriate interview methods and conducted all interviews using a semistructured interview guide. A qualitative methodology was used by applying a combination of 'open-ended' questions and probing techniques intended to elicit patients' own description of their experiences with BCC [21]. Interviews were conducted until saturation (or the point at which no new concepts emerged in the interview) was reached. Interview notes were systematically reviewed to enable continuous assessment of concepts over the course of the study and notes were tabulated to enable saturation to be assessed separately for each group of patients. Patients were asked to describe their cancer condition, current BCC-specific symptoms as well as HRQL impacts over the previous 7 days. Interviewers probed on each symptom mentioned, asking about intensity, severity, duration, bother, and any related limitations; understanding the impact of BCC-specific treatments was not within the scope of this research. Patients also provided demographic and BCC treatment information for descriptive purposes. A clinical form was completed for each patient by the site investigator (excluding patients who participated in the parallel interview study [I4J-MC-HHBB {1.3}]) outlining the length of time since BCC diagnosis, as well as prior and/or current therapies that patients were receiving for their BCC. All patients were reimbursed for their participation according to the fair market value based on the effort required for participation in the study.

### Data Analysis

Descriptive summary statistics were used to summarize demographic and clinical information. A content analysis approach [22] was used to analyze the data (based on notes, transcripts, and audio recordings) from the telephone interviews. A coding dictionary based on the semistructured interview guide was developed before completion of data collection to ensure that interview transcripts

were coded objectively and consistently. A qualitative analysis software program, ATLAS.ti (Muhr T. ATLAS.ti 5.0 edn. Berlin, Germany: ATLAS.ti Scientific Software Development GmbH; 2004), was used to organize and categorize systematically the text in the interview transcripts. Using a content analysis approach, the data were examined for general themes, as well as specific issues and concerns associated with BCC symptoms and impacts, with a focus on words or phrases that patients used to describe symptoms associated with the condition. All patient data for the analysis were deidentified before review by the sponsor of the study and co-authors.

## RESULTS

### Clinical and Demographic Characteristics

Thirty-four patient interviews were conducted (G1: $N = 13$; G2: $N = 21$). G1 comprised 11 patients with superficial subtype and two patients with nodular subtype BCC. G2 comprised 12 patients with metastatic BCC and nine patients with locally advanced BCC. Importantly, as data were collected, similar trends were observed in patient responses at an earlier time point for patients with non-advanced disease versus advanced disease; as a result, a smaller number of patients were recruited in G1.

The overall sample was mostly split between patients aged 55–64 years (32%, $N = 11$) and those aged 76+ years (32%, $N = 11$), and comprised primarily men (82%, $n = 28$). In G1, most patients (77%, $N = 10$) were older than 65 years, whereas, in G2, approximately half (48%, $N = 10$) were aged 55–64 years (Table 1). Almost half of the patients (47%, $N = 16$) were married or living with a partner and most patients (53%, $N = 18$) were retired or disabled. All patients had some form of health insurance, with more than half (59%, $N = 20$) using Medicare for coverage. Approximately half (56%, $N = 19$) reported having lived in a 'high-sun' area when they were 10–20 years old, although a greater proportion of patients in G1 (92%, $N = 12$) communicated that they were exposed to sun 'a lot' during that time compared with patients in G2 (57%, $N = 12$). A high-sun area was not defined by geographical location, but rather was based on patient self-report and investigator discretion. Although more patients in G1 (69%, $N = 9$) reported having frequent sunburns when younger, fewer in G1 (38%, $N = 5$) reported having skin that burned easily compared with those in G2 (47%, $N = 9$).

### Treatment History

Across both groups, most patients (84%, $N = 27$) had received pharmacologic therapy or had undergone procedures for BCC before the interview (Table 2). Surgical excision (53%, $N = 17$) and Moh's surgery (37%, $N = 12$) were the most common treatments received (by at least one-third of patients in each group). Almost half of the patients in G2 (47%, $N = 9$) had received vismodegib at some point previously. In terms of current treatment, most patients (75%, $N = 24$) were receiving some form of treatment, with almost equal amounts in both groups (G1: 77%, $N = 10$; G2: 74%, $N = 14$). Of those currently receiving treatment, vismodegib was the most common pharmacologic treatment at the time of their interview (19%, $N = 6$), which was recorded only for patients in G2, in line with the regulatory approved indication.

**Table 1** Patient demographic characteristics

| Characteristics | Total ($N = 34$) | Group 1: non-advanced ($N = 13$) | Group 2: locally advanced and/or metastatic ($N = 21$) |
|---|---|---|---|
| Age (years), *N* (%) | | | |
| 35–44 | 1 (3) | 0 (0) | 1 (5) |
| 45–54 | 3 (9) | 2 (15) | 1 (5) |
| 55–64 | 11 (32) | 1 (8) | 10 (48) |
| 65–75 | 8 (23) | 5 (38) | 3 (14) |
| 76+ | 11 (32) | 5 (38) | 6 (29) |
| Male gender, *N* (%) | 28 (82) | 10 (77) | 18 (86) |
| Marital status, *N* (%) | | | |
| Single, never married | 5 (15) | 0 (0) | 5 (24) |
| Married and/or living with partner | 16 (47) | 6 (46) | 10 (48) |
| Divorced | 9 (26) | 6 (46) | 3 (14) |
| Widowed | 4 (12) | 1 (8) | 3 (14) |
| Employment status, *N* (%) | | | |
| Employed, part-time | 2 (6) | 0 (0) | 2 (9) |
| Employed, full-time | 9 (26) | 4 (31) | 5 (24) |
| Retired | 16 (47) | 7 (54) | 9 (43) |
| Disabled | 2 (6) | 0 (0) | 2 (9) |
| Unknown | 5 (15) | 2 (15) | 3 (14) |
| Highest level of education completed, *N* (%) | | | |
| Less than high school | 2 (6) | 1 (8) | 1 (5) |
| GED/high-school equivalent | 4 (12) | 1 (8) | 3 (14) |
| Some college | 6 (18) | 1 (8) | 5 (24) |
| Graduated 2-year college | 3 (9) | 2 (15) | 1 (5) |
| Completed college degree | 7 (21) | 5 (38) | 2 (9) |
| Some postgraduate education | 1 (3) | 0 (0) | 1 (5) |
| Completed postgraduate degree | 9 (26) | 3 (23) | 6 (29) |
| Vocational training | 2 (6) | 0 (0) | 2 (9) |
| Type of insurance, *N* (%)[a] | | | |
| Medicare | 20 (59) | 9 (69) | 11 (52) |
| Medicaid | 2 (6) | 1 (8) | 4 (19) |
| Private health plan | 14 (41) | 5 (38) | 9 (43) |

**Table 1** continued

| Characteristics | Total ($N = 34$) | Group 1: non-advanced ($N = 13$) | Group 2: locally advanced and/or metastatic ($N = 21$) |
|---|---|---|---|
| Other insurance | 9 (26) | 6 (46)[b] | 3 (14)[c] |
| Location of residence during ages 10–20 years considered a high-sun area, *N* (%) | 19 (56) | 6 (46) | 13 (62) |
| Exposed to sun a lot between age of 10–20 years[d], *N* (%) | 24 (71) | 12 (92) | 12 (57) |
| Frequent sunburns when younger[d], *N* (%) | 17 (50) | 9 (69) | 8 (38) |
| Skin burns easily[d,e], *N* (%) | 14 (44) | 5 (38) | 9 (47) |

*ERP* extended reporting period, *GED* general education development, *MCE* medicaid coverage expansion, *VA* veterans health association

[a] Not mutually exclusive

[b] Other (*N*) includes VA System ($N = 5$) and ERP Supplement ($N = 1$)

[c] Other (*N*) includes VA System ($N = 1$), VA Health Insurance ($N = 1$), and MCE. On the county system ($N = 1$)

[d] Based on self-reported experience with sun exposure; responses included 'yes' responses only

[e] Does not include patients recruited from the NCT01226485 study ($N = 2$); denominator of $N = 32$ was used for this question

## Diagnosis and Perceived Severity of Disease

A greater proportion of patients in G2 (57%, $N = 12$) considered their condition to be more severe compared with patients in G1 (23%, $N = 3$). When characterizing the severity of their cancer, all patients mentioned the impact on their lifestyle and life expectancy, as well as the quantity and frequency of lesions appearing. In addition, patients in G2 discussed the emotional distress of the cancer when describing their disease severity, whereas patients in G1 did not. Three patients (G1: 8%, $N = 1$; G2: 9%, $N = 2$) had difficulty deciding on the severity of their cancer because of the discord between the severity reported by their doctor compared with their own understanding of their health and skin cancer condition. The way in which patients were first found to have BCC was almost identical in both groups, with the exception of three patients in G2, who reported waiting longer to seek treatment, thus resulting in more severe disease and greater impact, such as disfigurement. Most patients (G1: 61%, $N = 8$; G2: 67%, $N = 14$) sought medical care because of physical symptoms, such as lesions or bumps, which resulted in a diagnosis. Other patients (G1: 31%, $N = 4$; G2: 33%, $N = 7$) reported going to the doctor for unrelated reasons, such as a routine physical examination, when they were first found to have BCC.

Patients in both groups mentioned experiencing growths in similar locations on their bodies, such as their face, arms, chest, scalp, or head. Patients in G2 also reported lesions on their back and neck. Most patients (76%, $N = 16$) in G2 described their lesions as 'visibly apparent' to others, compared with 23% ($N = 3$) in G1. Patients in G2 also tended to experience more lesions at a given time and had a longer history of experiencing lesions.

**Table 2** Patient clinical characteristics

| Characteristics | Total ($N = 32$) | Group 1: non-advanced ($N = 13$) | Group 2: locally advanced and/or metastatic ($N = 19$) |
|---|---|---|---|
| Years receiving care at practice[a] | | | |
| Mean (SD) | 4.9 (6.8) | 4.4 (5.3) | 5.3 (7.8) |
| Range | 0.1–30.0 | 0.1–20.0 | 0.1–30.0 |
| Years since BCC diagnosis | | | |
| Mean (SD) | 8.0 (12.0) | 2.9 (6.8) | 11.4 (13.6) |
| Range | 0.0–43.0 | 0.0–24.0 | 0.0–43.0 |
| Previous treatment procedures, medication, or chemotherapy for BCC, *N* (%)[b] | | | |
| Yes | 27 (84) | 10 (77) | 17 (89) |
| Electrodessication and curettage | 2 (6) | 2 (15) | 0 (0) |
| Surgical excision | 17 (53) | 8 (61) | 9 (47) |
| Chemotherapy | 1 (3) | 0 (0) | 1 (5) |
| Radiation | 3 (9) | 0 (0) | 3 (16) |
| Vismodegib | 9 (28) | 0 (0) | 9 (47) |
| Pain medications | 1 (3) | 0 (0) | 1 (5) |
| Topical (5-FU, imiquimod) | 1 (3) | 1 (8) | 0 (0) |
| Moh's surgery | 12 (37) | 5 (38) | 7 (37) |
| Other[c] | 2 (6) | 0 (0) | 2 (10) |
| None | 5 (16) | 3 (23) | 2 (10) |
| Current treatment procedures, medication, or chemotherapy for BCC, *N* (%)[b] | | | |
| Yes | 24 (75) | 10 (77) | 14 (74) |
| Electrodessication and curettage | 1 (3) | 1 (8) | 0 (0) |
| Surgical excision | 5 (16) | 3 (23) | 2 (10) |
| Radiation | 1 (3) | 0 (0) | 1 (5) |
| Vismodegib | 6 (19) | 0 (0) | 6 (32) |
| Pain medications | 3 (9) | 1 (8) | 2 (10) |
| Topical (5-FU, imiquimod) | 2 (6) | 2 (15) | 0 (0) |
| Moh's surgery | 4 (12) | 2 (15) | 2 (10) |
| Other[d,e] | 7 (22) | 3 (23)[d] | 4 (21)[e] |
| None | 8 (25) | 3 (23) | 5 (26) |

Table does not include two patients from NCT01226485 clinical trial

*5-FU* fluorouracil, *PDT* photodynamic therapy, *SD* standard deviation

[a] Defined as the number of years a patients has been receiving care at the recruiting medical site

[b] Responses are not mutually exclusive

[c] Other ($N = 2$) includes clinical trial ($N = 1$) and fine-needle aspiration ($N = 1$)

[d] Other ($N = 3$) includes pending Moh's surgery in January 2014 ($N = 1$), shave biopsy ($N = 1$), and sunscreen ($N = 1$)

[e] Other ($N = 4$) includes arsenic trioxide ($N = 2$), following with oncologist ($N = 1$), and oculoplastics, ear, nose, throat (ENT) bone excision, and probably postoperative radiation ($N = 1$)

**Table 3** Patient-reported symptoms and impacts

| | Overall, *N* (%) | | |
|---|---|---|---|
| | **Total (*N* = 34)** | **Group 1: non-advanced (*N* = 13)** | **Group 2: locally advanced and/or metastatic (*N* = 21)** |
| Symptoms[a] | | | |
| Red lesions or open sores | 14 (41) | 7 (54) | 7 (33) |
| Cancer-related stress | 14 (41) | 5 (38) | 9 (43) |
| Itching localized to the lesion | 13 (38) | 6 (46) | 7 (33) |
| Pain related to cancer | 10 (29) | 0 (0) | 10 (48) |
| Bleeding lesions | 9 (26) | 4 (31) | 5 (24) |
| Problems sleeping | 8 (23) | 2 (15) | 6 (29) |
| Lack of energy | 3 (9) | 0 (0) | 3 (14) |
| Hair loss | 3 (9) | 1 (8) | 2 (9) |
| Depression | 2 (6) | 0 (0) | 2 (9) |
| Muscle cramps | 2 (6) | 0 (0) | 2 (9) |
| Dizziness | 1 (3) | 0 (0) | 1 (5) |
| Skin discoloration | 1 (3) | 1 (8) | 0 (0) |
| Impacts | | | |
| Daily activities | 22 (65) | 6 (46) | 16 (76) |
| Emotional well-being | 21 (62) | 6 (46) | 15 (71) |
| Social and/or leisure activities | 15 (44) | 4 (31) | 11 (52) |
| Cosmetic and functional | 14 (41) | 4 (31) | 10 (48) |
| Work and/or studies | 9 (26) | 2 (15) | 7 (33) |
| Personal relations | 9 (26) | 2 (15) | 7 (33) |
| Sexual activities | 5 (16) | 1 (8) | 4 (19) |

[a] Includes only patients who reported symptoms related specifically to their cancer; all treatment-related symptoms were excluded from the analysis and reporting

## Symptoms

The symptoms reported by patients were common across groups, and almost all patients in G1 (85%, $N = 11$) and G2 (95%, $N = 20$) were experiencing at least one symptom related to their BCC at the time of the current study (Table 3). Patients in G2 reported a larger number of different symptoms and a greater frequency of specific symptoms compared with patients in G1. The most frequently reported symptoms overall were red lesions or open sores that failed to heal (41%, $N = 14$) and cancer-related stress (41%, $N = 14$). Among

patients in G2, red lesions or open sores that failed to heal were more commonly reported by patients with locally advanced disease (38%, $N = 5/13$), whereas cancer-related stress was largely reported by patients with metastatic disease (75%, $N = 6/8$). Other commonly reported symptoms included itching localized to the lesion site (38%, $n = 13$), bleeding lesions (26%, $N = 9$), and problems sleeping (23%, $N = 8$). Pain related to cancer was frequently reported by G2 patients only (48%, $N = 10$).

At the conclusion of the interview, patients were asked which symptoms they considered the 'most bothersome'. Most patients in G2 (95%, $N = 20$) identified one or more symptoms as most bothersome compared with 69% ($N = 9$) of patients in G1. Patients in G1 ($N = 4$) had greater difficulty in identifying a bothersome symptom because they either had only one symptom or did not consider their symptoms to be bothersome. Across both groups, of the 29 patients who reported at least one bothersome symptom, the most commonly reported were cancer-related stress (24%, $N = 7$), itching localized to the lesion (24%, $N = 7$), and open sores that failed to heal (14%, $N = 4$) (Table 4).

## Impact

All patients were asked whether their BCC had impacted their daily activities, emotional well-being, social or leisure activities, work or studies, personal relations, or sexual activities over the previous 7 days. Table 3 summarizes this impact quantitatively.

### *Daily Activities*

A greater proportion of patients (76%, $N = 16$) in G2 reported experiencing some impact on daily activities compared with those in G1 (46%, $N = 6$). When asked how their cancer had affected their daily activities, 31% ($N = 4$) of patients in G1 and 57% ($N = 12$) of patients in G2 mentioned having to limit activities, such as exercise, strenuous activities, such as lifting heavy objects, or outdoor activities, to avoid sun exposure.

Patients in G2 (19%, $N = 4$) also mentioned experiencing fatigue, which limited their ability to complete chores or other household activities, whereas patients in G1 (31%, $N = 4$) mentioned needing to be more cautious when doing activities as a result of surgeries or symptoms. One patient in G1 and four patients in G2 mentioned having to change their schedules and daily activities because of doctor's appointments or when recovering from surgeries.

### *Emotional Well-Being*

Compared with G1, a greater proportion of patients in G2 reported being emotionally impacted by the disease (G1: 46%, $N = 6$; G2: 71%, $N = 15$). Approximately half of the patients in G2 (48%, $N = 10$) reported feeling self-conscious or embarrassed about their appearance because of the scarring or appearance of the lesions. Nineteen percent ($N = 4$) and 23% ($N = 3$) of patients in G2 and G1, respectively, mentioned being bothered by others staring at their lesions or scars.

Patients also reported being worried, stressed, or concerned about their health and the cancer (G1: 8% $N = 1$; G2: 24% $N = 5$) and being frustrated or upset with the reoccurrence of the cancer (G1: 15% $N = 2$; G2: 19%, $N = 4$). A few patients in G1 (15%, $N = 2$) and G2 (14%, $N = 3$) mentioned being depressed because of their cancer.

### *Social Impact*

About half of the G2 patients (52%, $N = 11$) and one-third of G1 patients (31%, $N = 4$) reported an impact on their social or leisure activities

**Table 4** Patient quotes regarding most bothersome symptoms

| Most bothersome symptoms | *N* (%)[a] | Group 1: non-advanced | Group 2: locally advanced and/or metastatic |
|---|---|---|---|
| Open sores that failed to heal | 4 (14) | "Yeah, it wouldn't heal over, like a—if you—if I'd jabbed it with a knife or something it would heal, but, uh, this was just a little sore that, uh, whenever I washed my face if it had any kind of a scab on there, it would come off and wouldn't heal." (Pt ID: 002-201) | "Yeah, an open bleeding wound, well, it would bleed sometimes and sometimes not. And, uh, it starts off a little slow, but just keeps growing bigger and bigger and eating more and more, uh, outward flesh." (Pt ID: 002-103)<br>"So it starts small and gets bigger and you said an open bleeding wound?" (Interviewer)<br>"Uh-huh [yes], the doctors call it moth eating, when the wound finally opens up, so that's how they describe it." (Pt ID: 002-103) |
| Cancer-related stress | 7 (24) | "Immediately around the time of being biopsied and finding the results, I'd say that for me is pretty severe. Now I'm just sort of waiting to get through the process, and then it's going to be very stressful the day of the surgery and the day after for sure. And then, it just sort of levels off again." (Pt ID: 003-201)<br>"I'd say stress related to the cancer is the most bothersome and biggest issue…there's an unknown component whether it's going to heal or not and whether it's going to leave physical scars or not." (Pt ID: 001-208) | "Um, when I get upset because of the stress, uh, it—it becomes—you know, yes, I'm bothered by it. On, uh, a daily thing when I'm not doing anything great or anything and I don't get worked up, uh, I think the, uh, medication works fine and I can control it. But it's just when things start going backwards, which they do quite a lot, um, then it starts becoming an issue." (Pt ID: 002-103)<br>"Probably—at this point, probably the stress of the unknown because I know the itching will go away and the redness will go away." (Pt ID: 002-111) |
| Itching localized to the lesion | 7 (24) | "Um, I have itching or, um, a discomfort, it's like, uh, a sore or a mosquito bite or something that's there, you know." (Pt ID: 001-204)<br>"It—uh, it's bothersome, you know, it's like any itch you have, you want to scratch it. You know you shouldn't in this case and that—that's what's, uh, the bother really." (Pt ID: 002-201) | "Itching and—uh, itching and burning because that causes—when I rub that it causes it to bleed. You know, even if you rub on the side of it or something, uh, then the scab comes off. So the itching is what triggers it." (Pt ID: 003-105) |

The symptoms listed were described by patients as their most bothersome symptoms during the interview discussion
*Pt ID* patient identifier
[a] A denominator of 29 was used to calculate the percentages; this is based on the total number of patients who reported at least one 'most bothersome' symptom

**Table 5** Patient quotes regarding impacts and change in behavior

| Impact on HRQL | Group 1: non-advanced | Group 2: locally advanced and/or metastatic |
|---|---|---|
| Daily activities | "Well, like, right now because this is still a bit of an open wound, you know, I have to be careful I, you know, don't pump my heart rate up too high at the gym and things like that." (Pt ID: 003-201) | "Well, I'm stuck inside, like I said. I—I mean, I can jump in the car and go to the store and stuff. But I'm limited to doing normal things of going outside, maybe going to a—to a baseball game, or going to the park and just going…for a walk. I can't do any of those things." (Pt ID: 001-018) |
| Emotional well-being | "Uh, I'm tired of having my body cut. I mean, you could say it's at times mildly depressing." (Pt ID: 001-205) | "You know, I know it's, now that I know what it is, I want to get rid of it. But, I know other people see it on my skin and wonder what that is. I don't know." (Pt ID: 001-103)<br>"Well, I don't—I don't like it when people stare at me. Um, it makes me a little bit uneasy; especially the little children. That bothers me." (Pt ID: 001-016) |
| Social impact | "Yeah, I'm not as motivated, you know, I just—I'm tired, uh, when you're not sleeping you don't have that energy to go—to go out there and—and do those things [hiking with dog or going snowshoeing with friends]. I—I try to push myself too when I have a good days, but there's been a lot more bad days." (Pt ID: 002-202) | "I don't know if it's leisure, but it's basically all the yard work. Back when they were open sores it would stop [me from] meeting people—talking to people and basically staying in." (Pt ID: 002-108) |
| Cosmetic and functional impact | "Well, I wear the hat and the wig because after all these surgeries I—I have no hair, it's all scar tissue and [sigh] I think my mind has shut down." (Pt ID: 002-202) | "Uh, a great, gaping wound on my face and no ears, I mean as soon as you look at me you can tell something is definitely wrong with this guy." (Pt ID: 002-103) |
| Change in behavior | "Um, the only change in lifestyle that I've done, as a result of the cancers, is I am much more aware of being in the sun without some sort of protection." (Pt ID: 001-205) | "I might go outside and that sun hits this open wound on the side of my face it's just like putting it in a fry pan. I always wear a great big broad brim hat and stuff, um, when I go outside." (Pt ID: 002-103) |

*HRQL* health-related quality of life, *Pt ID* patient identifier

because of their cancer. The most common reasons included having to reduce outdoor activities (G1: 15%, $N = 2$; G2: 24%, $N = 5$), such as hiking, gardening, and going to watch baseball games, as well as spending less time with friends and family (G1: 23%, $N = 3$; G2: 24%, $N = 5$) because of their appearance. Patients also reported that the time spent

receiving medical treatment (including transportation) limited their activities.

***Cosmetic and Functional Impact***

Cosmetic and functional impacts resulting from cancerous lesions or cancer-related surgeries were described by patients in both groups. Almost half of G2 patients (48%, $N = 10$) described functional and cosmetic impacts, such as visible scarring (9%, $N = 2$), malformation of the skin because of the cancerous lesions (24%, $N = 5$), or having part or all of a body part (i.e., ears or eyes) removed because of surgery (19%, $N = 4$). One-third of patients in G1 (31%, $N = 4$) were concerned with the need for repeat surgeries and the potential for scarring, especially in places on the body that were highly visible to others. Patients across both groups also communicated a feeling of fear, stress, and embarrassment associated with the cosmetic and functional impacts.

**Changes in Behavior**

Changes in behavior were reported almost equally across both groups (G1: 100%, $N = 13$; G2: 91%, $N = 10/11$); limitations on sun exposure were reported most commonly (G1: 92%, $N = 12$; G2: 82%, $N = 9/11$). Almost half of the patients in both groups (G1: 38%, $N = 5$; G2: 48%, $N = 10$) reported wearing additional clothing to protect themselves from the sun and wearing a hat when going outside (G1: 31%, $N = 4$; G2: 24%, $N = 5$). Patients also reported reducing or limiting sun exposure by wearing sunscreen or seeking shaded areas.

A few patients in both groups (G1: 15%, $N = 2$; G2: 36%, $N = 4/11$) mentioned having to alter their clothing as a result of their surgeries by wearing more loosely fitted clothing or wearing clothing to hide a symptom of the cancer, such as a red lesions or open sores.

Select patient quotations characterizing BCC-specific impacts and changes in behavior affecting HRQL are documented in Table 5.

## DISCUSSION

Although several efforts have been made to determine the impact of NMSC on HRQL, few studies have examined the specific impact of BCC. This study was conducted to generate descriptive information specific to BCC. Importantly, patients with either non-advanced or locally advanced or metastatic BCC experienced symptoms and impacts from their disease that affected their HRQL. Although there were some commonalities between the two groups, there were some key differences that are important to highlight.

Overall, a greater proportion of patients with locally advanced or metastatic disease deemed their condition to be severe compared with patients with non-advanced disease. Patients in G2 were more likely to describe frequent and bothersome symptoms and expressed experiencing a greater HRQL impact across six of the seven categories evaluated compared with patients in G1. Pain related to cancer was reported by approximately half of G2 patients, whereas it was not reported by any patient in G1. Similar to Mathias et al. [19], the current study found that impacts on emotional well-being and daily activities were common and more frequently reported in patients with more advanced disease. Consistent with Shingler et al. [10], the current study also found that BCC imposes a significant psychological and cosmetic burden on patients, as demonstrated by approximately 50%

of G2 experiencing visible scarring, malformation of the skin, or loss of a body part.

Although more subtle, disease stages that are non-advanced can impose bothersome sequelae and negative impacts on patients' HRQL. Despite the relatively small sample size of G1, approximately half of patients reported the disease as having a negative impact on their emotional well-being and daily activities. In addition, anxiety related to potential or existing scarring, as well as tumor recurrence, was communicated by one-third of the sample.

These findings, similar to those of Burdon-Jones et al. [18], suggest that, although the burden can be less when compared with those with more advanced disease, it is important to assess HRQL in all patients with BCC. In our study, the domains or themes that emerged as the most important to assess a patient's HRQL across both groups included cosmetic and functional impacts, emotional well-being, and changes in behavior and daily activities to avoid sun exposure. These domains, particularly the fear of scaring and disfigurement and the importance of avoiding excess sun, also corresponded to the important themes identified by Burdon-Jones et al. [18], providing additional evidence to support the impact of these domains in the BCC patient population.

In addition, the findings from this study also suggest that, although is it important to evaluate the HRQL in both groups of patients, different aspects of the HRQL domains are more relevant based on the stage of the disease. For example, the impact on daily activities is an important domain to measure in both populations. Most patients with non-advanced disease experienced cutaneous surface-level symptoms, such as red spots or localized itching, which tended to affect daily activities that pertained to limiting sun exposure or modifying clothing selections. However, in patients with more advanced disease, the daily activities affected were changes in lifestyle, such as the inability to clean the house or reductions in exercise. Based on these differences, PROs in the local disease population should focus on these initial behavioral changes in terms of daily impact, whereas patients with advanced disease should be more broadly assessed, given the number of activities limited by their condition.

In addition, because of the number of patient comments regarding healthcare utilization and time burden, it would be useful to examine the healthcare resource utilization in both patient groups to gain a better understanding of the economic and time burden associated with BCC. Many patients were currently undergoing treatment at the time of the interviews, and both patient groups mentioned the burden associated with treatment, such as scheduling appointments, the cost of the procedures, and reduced or loss of productivity while recovering from surgery.

Although the study was intended to characterize the patient population, several limitations should be considered when interpreting these results. Patients for both groups were difficult to recruit. Given the accessibility and effectiveness of surgery in those with non-advanced disease, many eligible patients did not have current baseline disease and were ineligible for the study. This requirement of measurable disease, however, reduced the possibility of recall bias which could otherwise have been considered as an additional limitation to these results. Likewise, the recruitment of patients with locally advanced and metastatic disease was difficult because of the rarity of this advanced disease stage. This resulted in a long recruitment period for a limited number of interviews and a sample of patients from only two states (California and

Michigan), which decreases the generalizability of these results. In addition, because of the difficulty in recruiting patients, all qualitative interviews were conducted over the telephone and not in person. Although not ideal for facilitating communication between patients and interviewers, conducting qualitative interviews by telephone did enable increased patient participation, especially for those patients who had progressive disease or were older and being cared for by another. Other limitations that should be taken into consideration include the relatively few female participants, as well as other variables not controlled for in this study that could inform patients' impressions of their disease (i.e., education regarding BCC, experience of family or friends with BCC, or impact of treatments).

A strength of the study was the use of qualitative methodology, which enabled exploration of concepts with patients in a not well-understood population. In addition, conducting interviews with patients at varying stages of disease provided an understanding of HRQL along the progression of disease, which has not been previously done.

This study provides insight into a patient population that has not previously been well defined in the literature. Future studies with a broader scope might be interested in highlighting similarities and/or differences between BCC and other types of skin malignancy in terms of disease symptoms and HRQL impact. Although the information gained from this study fills a gap in the scientific literature and supports the development of measurements to evaluate new therapies, studies in larger numbers of patients with BCC (including a greater proportion of women) are warranted to refine the concepts most relevant to this population of patients.

## CONCLUSION

Patients with non-advanced or locally advanced and metastatic BCC experience disease-related symptoms that affect their HRQL, activities of daily living, emotional well-being, and social and/or leisure activities. Providing this patient perspective on important symptoms and HRQL impact helps to more broadly characterize the influence of different disease stages of BCC on the daily life of patients and provides a foundation for additional refinement of concepts most relevant to them.

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***Compliance with ethics guidelines.*** All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964, as revised in 2013. Informed consent was obtained from all patients for being included in the study.



## REFERENCES

1. Madan V, Lear JT, Szeimies RM. Non-melanoma skin cancer. Lancet. 2010;375:673–85.
2. Katalinic A, Kunze U, Schafer T. Epidemiology of cutaneous melanoma and non-melanoma skin cancer in Schleswig-Holstein, Germany: incidence, clinical subtypes, tumour stages and localization (epidemiology of skin cancer). Br J Dermatol. 2003;149:1200–6.
3. Staples MP, Elwood M, Burton RC, et al. Non-melanoma skin cancer in Australia: the 2002 national survey and trends since 1985. Med J Aust. 2006;184:6–10.
4. Donaldson MR, Coldiron BM. No end in sight: the skin cancer epidemic continues. Semin Cutan Med Surg. 2011;30:3–5.
5. Diffey BL, Langtry JA. Skin cancer incidence and the ageing population. Br J Dermatol. 2005;153:679–80.
6. Erba P, Farhadi J, Wettstein R, et al. Morphoeic basal cell carcinoma of the face. Scand J Plast Reconstr Surg Hand Surg. 2007;41:184–8.
7. Miller SJ, Alam M, Andersen J, et al. Basal cell and squamous cell skin cancers. J Natl Compr Canc Netw. 2010;8:836–64.
8. National Comprehensive Cancer Network. Basal and Squamous Cell Skin Cancer (Version 1.2014).

http://www.nccn.org/professionals/physician_gls/pdf/nmsc.pdf. Accessed July 13, 2015.

9. Nunes DH, Frode TS. Quality of life in basal cell carcinoma patients in Brazil: a pilot cross sectional study. Dermatol Surg. 2013;39:620–6.

10. Shingler SL, Garside J, Samanta K, et al. Utilities for advanced basal cell carcinoma. J Med Econ. 2013;16:777–83.

11. Caddick J, Green L, Stephenson J, Spyrou G. Psychological outcomes following surgical excision of facial skin cancers. Eur J Plast Surg. 2013;36:75–82.

12. Chren MM, Sahay AP, Bertenthal DS, et al. Quality-of-life outcomes of treatments for cutaneous basal cell carcinoma and squamous cell carcinoma. J Invest Dermatol. 2007;127:1351–7.

13. Lee EH, Klassen AF, Nehal KS, et al. A systematic review of patient-reported outcome instruments of nonmelanoma skin cancer in the dermatologic population. J Am Acad Dermatol. 2013;69:e59–67.

14. Rhee JS, Matthews BA, Neuburg M, et al. Skin cancer and quality of life: assessment with the Dermatology Life Quality Index. Dermatol Surg. 2004;30:525–9.

15. Blackford S, Roberts D, Salek MS, Finlay A. Basal cell carcinomas cause little handicap. Qual Life Res. 1996;5:191–4.

16. Lee KC, Weinstock MA, Veterans Affairs Topical Tretinoin Chemoprevention Trial G. Prospective quality of life impact of keratinocyte carcinomas: observations from the Veterans Affairs Topical Tretinoin Chemoprevention Trial. J Am Acad Dermatol. 2010;63:1107–9.

17. Rhee JS, Matthews BA, Neuburg M, et al. Validation of a quality-of-life instrument for patients with nonmelanoma skin cancer. Arch Facial Plast Surg. 2006;8:314–8.

18. Burdon-Jones D, Thomas P, Baker R. Quality of life issues in nonmetastatic skin cancer. Br J Dermatol. 2010;162:147–51.

19. Mathias SD, Chren MM, Colwell HH, et al. Assessing health-related quality of life for advanced basal cell carcinoma and basal cell carcinoma nevus syndrome: development of the first disease-specific patient-reported outcome questionnaires. JAMA Dermatol. 2014;150:169–76.

20. Edge S, Byrd DR, Compton CC, et al., editors. American Joint Committee on Cancer (AJCC) Cancer Staging Manual. 7th ed. New York: Springer; 2010.

21. Patrick DL, Burke LB, Gwaltney CJ, et al. Content validity–establishing and reporting the evidence in newly developed patient-reported outcomes (PRO) instruments for medical product evaluation: ISPOR PRO good research practices task force report: part 1–eliciting concepts for a new PRO instrument. Value Health. 2011;14:967–77.

22. Hsieh H-F, Shannon SE. Three approaches to qualitative content analysis. Qual Health Res. 2005;15:1277–88.