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# Keratinocyte Carcinoma: Canadian Landscape and an Evidence-based Approach to Follow-up

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## Introduction

Dermatologists play a vital role in the early detection, prevention and effective management of skin cancer in patients with a prior history of the disease. Regular monitoring and timely interventions greatly enhance the overall prognosis and quality of life for patients with skin cancer. Dermatologists possess the requisite expertise to accurately diagnose and oversee the management of cutaneous skin cancers.

Skin cancer screening via total body skin exam (TBSE) is often considered one of the safest, easiest, and most cost-effective tests in medicine.[1] Despite dermatologists' ability to offer such invaluable care for this patient population, offering routine skin checks for all patients with a prior history of skin cancer becomes exceptionally challenging given the high demand for dermatology care across Canada. It is important for dermatologists to maximize the efficiency of care during TBSEs by adhering to evidence-based guidelines when determining the frequency and duration of follow-up. These guidelines also provide a solid foundation for discussions with patients regarding the rationale for discharge back to their primary care provider.

## Skin Cancer as a Chronic Disease

By its definition, a condition qualifies as a chronic disease if it lasts for more than one year, necessitates continuous medical attention, and/or restricts activities of daily living.[2] Skin cancer as a chronic disease is a novel concept that aims to provide a more comprehensive understanding of skin cancer patients experiencing considerable morbidity due to their condition, requiring heightened healthcare resources.[3]

A population-based study conducted in Canada revealed that the incidence of keratinocyte carcinoma (KC), encompassing both squamous cell carcinoma (SCC) and basal cell carcinoma (BCC), increased by

30% between 2003 and 2017.[4] Furthermore, about 60% of patients with a history of KC will develop another carcinoma within 10 years.[5] After a primary BCC, 50% of patients will have at least one more BCC within 5 years.[6,7] Similarly, there is a 42% risk of a second SCC within 5 years, increasing to 72% for those with two or more SCCs.[5]

## Epidemiology of Keratinocyte Carcinoma in Canada

The epidemiology of SCC and BCC in Canada reveals a significant burden of KC, although reported data is limited. A retrospective analysis by Jung et al. on 98,645 patients in Alberta from 1988 to 2007 reported 66,192 cases of BCC (34,825 males and 31,367 females), 12,494 cases of SCC *in situ* (6,106 males and 6,388 females), and 19,959 cases of invasive SCC (12,315 males and 7,644 females).[8] Another study by Tang et al. from the Ontario health administrative database (ICES) highlighted an increase in the incidence and mortality of KC from 1998 to 2017, with the incidence rising from 328.6 to 356.7 per 100,000 adults and the annual mortality rate increasing 4.8-fold from 6.39 to 30.53 deaths per 1,000,000 adults.[9]

Adding to this data, Hayes et al. examined KC cases in New Brunswick between 1992 and 2001, identifying 8,550 new cases of BCC (4,513 males and 4,037 females) and 3,036 new cases of invasive SCC (1,851 males and 1,185 females).[10] When age-standardized to the 2000 world population, the incidence rates per 100,000 population were 86.9 for males and 67.7 for females for BCC, and 34.0 for males and 16.1 for females for invasive SCC. The study also

| Source | Location | Recommendations |
|---|---|---|
| Peris et al, 2023[12] *European Association of Dermato-Oncology* | Europe | **Low-risk:** No follow-up<br>**High-risk:** Every 12 months for at least 3-5 years |
| National Comprehensive Cancer Network, 2024[13] | United States | **All risks:** Every 6 months year 1-5, every 12 months thereafter for life |
| Nasr et al, 2021[14] *British Association of Dermatologists* | United Kingdom | **Low-risk:** No follow-up<br>**High-risk:** Every 6 months year 1, every 12 months starting year 2 for 5-10 years |
| Zloty et al, 2015[15] *Canadian Non-melanoma Skin Cancer Guidelines Committee* | Canada | **Low-risk:** Yearly (duration not reported)<br>**High-risk:** Every 6 months year 1-3, every 12 months starting year 4 (duration not reported) |

**Table 1.** Follow-up recommendations for basal cell carcinoma from major dermatologic associations; *courtesy of Jorge R. Georgakopoulos, MD, FRCPC*

| Source | Location | Recommendations |
|---|---|---|
| National Comprehensive Cancer Network, 2024[16] | Unites States | **Low-risk:** Every 3-12 months for year 1-2, every 6-12 months year 3-5, every 12 months thereafter for life<br>**High-risk:** Every 3-6 months for year 1-2, every 6-12 months year 3-5, every 12 months thereafter for life |
| Alam et al, 2018[17] Invited working group | United States | **All risks:** At least yearly (duration not reported) |
| *Keohane et al, 2021[18] British Association of Dermatologists* | United Kingdom | **Low-risk:** 1 post-treatment visit only<br>**High-risk:** Every 4 months year 1, every 6 months year 2 then stop |
| *Stratigos et al., 2020[19] European Association of Dermato-Oncology* | Europe | **Low-risk:** Every 6-12 months for 5 years<br>**High-risk:** Every 3 months year 1-2, every 6 months 1-5, every 12 months thereafter for life |

**Table 2.** Follow-up recommendations for squamous cell carcinoma from major dermatologic associations; *courtesy of Jorge R. Georgakopoulos, MD, FRCPC*

revealed that the lifetime probability of developing BCC in New Brunswick was approximately 13%, with a 5% probability of developing invasive SCC. BCC accounted for approximately 74% of KC in this population, with a BCC to invasive SCC ratio of 2.8 to 1. These findings collectively underscore the growing public health challenge posed by SCC and BCC across Canada.

## Follow-up Guidelines from Major Dermatologic Organizations

There are numerous guidelines from dermatologic associations worldwide for the follow-up of patients with a history of KC.[11] Post-treatment follow-up is designed to detect recurrence and metastasis, monitor for new primary tumors, and reinforce ongoing preventive behaviours. There remains uncertainty about the optimal frequency for follow-up skin examinations after KC treatment, which has significant implications for both patient outcomes and healthcare resources. Herein, we summarize the available practice guidelines from major dermatologic associations to provide dermatologists with an evidence-based framework for follow-up care, helping them reflect on whether their current follow-up practices are sufficient or excessive.

*Basal cell carcinoma* **(Table 1)**: Follow-up guidelines for BCC vary across various regions and organizations. According to the European Association of Dermato-Oncology, low-risk BCC requires no follow-up, while high-risk cases should be monitored every 12 months for at least 3-5 years. The National Comprehensive Cancer Network in the United States recommends follow-up every 6 months during the first 5 years for all risk levels, then annually for life. The British Association of Dermatologists suggests no follow-up for low-risk BCC, with high-risk patients being seen every 6 months in the first year, then annually for 5-10 years. In Canada, the Non-Melanoma Skin Cancer Guidelines Committee advises yearly follow-up for low-risk BCC and more frequent follow-up for high-risk cases, with every 6 months for the first 3 years, and then annually starting in year 4, although the duration is not specified.

*Squamous cell carcinoma* **(Table 2)**: Follow-up guidelines for SCC differ based on risk levels and regional practices. The National Comprehensive Cancer Network (NCCN) in the United States advises more

| | |
|---|---|
| Tumour specific factors | Aggressive subtype, large tumours, recurrence, and location (head and neck; eye, ear, nose or mouth) |
| Non-modifiable individual factors | Skin pigmentation/type, hair colour, eye colour. |
| Environmental | Lifetime sun exposure, sunbathing frequency before age 30, tanning bed usage, living at low latitudes and high elevation during both childhood and adult life, recreational activities and environmental pollutants. |
| Iatrogenic | Long-term immunosuppressive therapy (i.e., organ transplantation, autoimmune conditions, autoinflammatory conditions, HIV/AIDs), radiation therapy, psoralen and ultraviolet A (PUVA) therapy, biologic therapy, and chronic wound healing. |
| Occupation | Individuals engaged in occupations for a prolonged period of time with extended exposure to radiation (ultraviolet or man-made) and chemicals; including but not limited to outdoor jobs, airline pilots and crew, farmers and agricultural workers, fisherman, construction workers, and military personnel. |
| Genodermatosis | Xeroderma pigmentosum, basal cell nevus syndrome (Gorlin syndrome), oculocutaneous albinism (OCA), epidermodysplasia verruciformis, dyskeratosis congenita, Bazex-Dupré-Christol syndrome, epidermolysis bullosa, Bloom syndrome, Rombo syndrome, Fanconi anemia, Ferguson-Smith syndrome. |
| Field cancerization | Phenomenon in which a large area of tissue is affected by genetic and epigenetic alterations, making it more susceptible to the development of multiple skin cancers. This concept suggests that the entire field of tissue surrounding a primary tumor may be at risk for the development of additional tumors, even if they are not clinically visible.[20,21] |

**Table 3.** Complex skin cancer in context of keratinocyte carcinomas; *courtesy of Jorge R. Georgakopoulos, MD, FRCPC*

frequent follow-ups for high-risk patients, ranging from every 3-6 months in the first 2 years to annually for life, while low-risk patients are monitored less frequently. In contrast, the British Association of Dermatologists recommends just one post-treatment visit for low-risk SCC, with high-risk patients receiving more regular check-ups in the first 2 years before follow-up stops. The European Association of Dermato-Oncology suggests frequent follow-ups for high-risk cases, especially in the first 2 years, tapering to annual visits after 5 years.

**Table 3** summarizes the key patient factors dermatologists should consider when identifying individuals with complex skin cancer. The term 'complex skin cancer' refers to a multifaceted spectrum of conditions, encompassing patients with skin cancer who are at a heightened risk for future cutaneous malignancy. This complexity underscores the need for specialized and comprehensive approaches in both diagnosis and management by dermatologists and allied health professionals. These factors should be carefully considered when determining follow-up intervals.

## Conclusion

The management of KC in Canada demands a nuanced approach, especially in light of the rising incidence of the disease. Data shows a significant increase in KC cases, with incidence rates climbing over the past decades. As dermatologists play a crucial role in providing continuous care for these patients, the growing demand for dermatology services across Canada poses a challenge. The lack of consensus on follow-up guidelines further complicates this issue, requiring dermatologist to utilize guidelines based on their unique clinical practice and regional healthcare landscape. In the future, establishing standardized follow-up protocols is essential to optimize patient outcomes while managing the increasing strain on dermatology care.

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## Financial Disclosures

**None declared.**

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