



PhD Thesis
Johan Sieborg

Epidemiological Insights into Keratinocyte Carcinoma: From Incidence to Clinical Outcomes

Principal supervisor: Merete Hædersdal

Primary co-supervisor: Alexander Egeberg

Co-supervisors: Emily Wenande, Ulrikke Lei

This thesis has been submitted to the
Graduate School of Health and Medical Sciences,
University of Copenhagen, January 31, 2026

PhD Thesis

Author

Johan Sieborg

Department

Bispebjerg Hospital, Department of Dermatology

Title

Epidemiological Insights into Keratinocyte Carcinoma: From Incidence to Clinical Outcomes

Submitted

This thesis has been submitted to the Graduate School of Health and Medical Sciences, University of Copenhagen, January 31, 2026

Principal supervisor

Prof. Merete Hædersdal, MD, PhD, DMSc
Department of Dermatology,
Bispebjerg Hospital,
University of Copenhagen

Primary co-supervisor

Prof. Alexander Egeberg, MD, PhD, DMSc
Department of Dermatology,
Bispebjerg Hospital,
University of Copenhagen

Co-supervisors

Ulrikke Lei, MD.
Department of Dermatology,
Gentofte Hospital

Emily Wenande, MD, PhD.
Department of Dermatology,
Bispebjerg Hospital

Chairman

Associate prof. Beatrice Dyring-Andersen, MD, PhD.
Department of Immunology and Microbiology,
University of Copenhagen, Denmark

Opponents

Prof. Peter Bjerring, MD, PhD.
Aalborg University/Aalborg University Hospital, Denmark

Andrés Metz Erlendsson, MD, PhD.
Department of Dermatology,
Karolinska University Hospital, Sweden

Abstract

The incidence of most common skin cancer, keratinocyte carcinoma (KC), is increasing worldwide, and projections indicate that this trend will continue. Although KCs have a low mortality rate, they impose a substantial disease burden due to the sheer numbers and the fact that many patients develop multiple KCs. Further, removal of KCs located in high-risk anatomical areas—such as nose, ear, and eyelids—can result in visible scarring and severely disfiguring surgery with loss of function. KC can be subdivided into basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). The two most common BCC subtypes are nodular BCC (nBCC) and superficial BCC (sBCC). SCC has known precursors, including actinic keratosis (AK) and Bowen’s disease (BD), which differ mainly in the extent of epidermal involvement. Most epidemiological studies focus only on BCC and SCC, overlooking important nuances between specific BCC subtypes and SCC precursors. From a clinical perspective, KC subtype guides which treatment is selected and epidemiological studies should reflect these subtype differences to accurately determine disease burden.

The aim of this PhD thesis was to assess the KC burden in Denmark for nBCC, sBCC, SCC, and BD as well as evaluate treatment outcomes for nBCC and sBCC. This was achieved over three studies where: Study I determined the incidence and lifetime risk for developing at least one KC/BD; Study II examined how socioeconomic-status (SES) and distance to a dermatological clinic were associated to incidence and tumour size; Study III examined and compared BCC recurrence following different treatment modalities, as well as to examining recurrence predictors with machine learning.

The studies in this thesis primarily use the Danish Skin Cancer Registry that contains information about KC tumours treated in office-based dermatological practices during 2013–present,

including treatment, tumour characteristics, subtypes, information related to control visits, and recurrence tumours. Study I and II used the Danish Skin Cancer Registry covering 2013–2022, whereas Study III used an updated Danish Skin Cancer Registry with data up to 2024.

The results from Study I showed that national KC incidence increased substantially by 172% between 2013 and 2022, with an increasing incidence trend found for each KC subtype (nBCC, sBCC, SCC, and BD). Moreover, the lifetime risk of developing at least one KC/BD was estimated at 21.8%. In Study II, it was found that individuals with high SES had significantly higher KC incidence (BCC incidence rate ratio: 2.4–2.7, SCC incidence rate ratio: 2.1) and smaller tumours (nBCC: –9.5%, sBCC: –8.5%, SCC: –11.3%, BD: –13.9%) than individuals with low SES. Additionally, SCC incidence increased with greater distance to a dermatological clinic, whereas nBCC incidence decreased with distance. Finally, Study III determined recurrence rates and hazard rate ratios for different nBCC and sBCC treatment modalities, showing that standard excision had the lowest recurrence rate for nBCC (8-year cumulative recurrence rate (CRR): 16.6%), whereas both standard excision and curettage had similar recurrence for sBCC (both had an 8-year CRR of 16.3%). Furthermore, short distance to a dermatological clinic and a high number of hospital registered diagnoses were found to be predictors of 2-year BCC recurrence.

Collectively, these studies deepen our epidemiological understanding of KC subtypes and their burden of disease in Denmark, which is especially important for resource allocation and prevention initiatives. Moreover, determining recurrence rates and comparing treatment modalities, along with assessing how BCC recurrence is affected by non-tumour-related factors, provides valuable insights for clinical guidelines and BCC management. The findings lay the foundation for future studies investigating KC patient characteristics, potentially using cluster analysis, as well as more in-depth analyses of specific treatments, such as determining the optimal excision margin.

Dansk resumé | Danish summary

Incidensen af almindelig hudkræft, også kaldet keratinocytcarcinom (KC), er globalt set steget markant, og nye prognoser estimerer, at denne tendens vil fortsætte. KC har en lav dødelighed, men grundet den store mængde individer, som udvikler KC årligt, har denne kræfttype en stor sygdomsbyrde for sundhedssektoren. Derudover kan excision af KC, specielt i højrisiko anatomiske områder som øre, næse, øjenlåg, resultere i betydelige, synlige ar eller føre til tab af funktion af disse strukturer. KC kan inddeles i to hovedgrupper: basalcellekarcinom (BCC) og plade-cellekarcinom (SCC). Den langt hyppigste undertype er BCC, som yderligere kan opdeles i nodulær BCC (nBCC), superficial BCC (sBCC), samt andre sjældnere BCC-undertyper. Kendte SCC-forstadier inkluderer Bowen's sygdom (BD) og aktinisk keratose (AK), som primært adskiller sig i graden af involvering af epidermis. Typisk udføres epidemiologiske studier på BCC, hvilket medfører tab af mere nuanceret information om de specifikke BCC-undertyper. Fra et klinisk perspektiv har den specifikke KC-undertype enorm betydning for behandlingsvalget og epidemiologiske studier bør derfor afspejle dette.

Formålet med denne PhD afhandling var at bestemme sygdomsbyrden af KC i Danmark for nBCC, sBCC, SCC og BD samt undersøge forskellige behandlinger af nBCC og sBCC. Dette blev gjort over tre studier hvor: Studie I bestemte udbredelsen og livstidsrisikoen af KC; Studie II undersøgte, hvordan socioøkonomiske status og afstanden til dermatologiske klinikker var associeret med incidensen og tumorstørrelser af KC; Studie III undersøgte og sammenlignede revidiv af BCC efter forskellige behandlingsmodaliteter samt identificerede recidivprediktorer ved hjælp af maskinlæring.

De epidemiologiske studier i denne PhD-afhandling anvender det detaljerede hudkræftregister: Hudkræftdatabasen. Databasen omfatter KC tumorer behandlet hos praktiserende speciallæger

i perioden 2013 til i dag og indeholder blandt andet oplysninger om behandlingsvalg, tumor karakteristika, KC undertype, samt information om kontrolbesøg og recidiv tumorer. Studie I og II brugte data fra Hudkræftdatabasen for perioden 2013–2022, mens i Studie III blev anvendt opdaterede data fra samme database frem til 2024.

Resultaterne fra Studie I viser, at incidensen for nBCC, sBCC, SCC og BD er steget betydeligt, med en samlet national stigning af KC på 172% fra 2013–2022. Derudover blev livtidsrisikoen for at udvikle mindst en KC udregnet til hele 21.8%. I Studie II fandt vi, at incidensen var højere (BCC incidensrate ratio: 2.4–2.7, SCC incidensrate ratio: 2.1) og tumorer var mindre (nBCC: –9.5%, sBCC: –8.5%, SCC: –11.3%) blandt individer med høj socioøkonimisk status sammenlignet individer med lav socioøkonimisk status. Afstand til klinikker havde forskellig effekt: SCC incidensen steg med længere afstand, mens nBCC incidensen faldt. Endeligt viste Studie III, at recidivrate var lavest efter behandling med standard excision for nBCC (8-års kumulativ recidivrate: 16.6%), mens for sBCC var det både standard excision og afskrabning (begge havde en 8-års kumulativ recidivrate på 16.3%). Derudover havde de ikke-tumorer-relaterede faktorer, afstand til klinikker og antallet af hospital-registreret diagnoser, en væsentlig betydning for prediktion af recidiv tumorer inden for 2 år efter behandling.

Samlet set giver studierne en overordnet forståelse for den sygdomsbyrde, KC udgør for vores sundhedssektor i Danmark, hvilket er enormt vigtigt for ressourceallokering og for at forstå sygdomsmønstre til brug i solbeskyttelses- og oplysningskampagner. Desuden er tiden til recidiv efter forskellige behandlinger blevet estimeret, hvilket kan være værdifuldt for både behandlingsvalg og udarbejdelsen af BCC-retningslinjer. Studierne danner grundlag for fremtidige undersøgelser af patientkarakteristika og mere dybdegående analyser af specifikke behandlinger, såsom at bestemme den optimale excisionsmargin.