

## ORIGINAL RESEARCH

## Defining the incidence of cutaneous squamous cell carcinoma in coastal NSW Australia

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## ABSTRACT

**Background/Objectives:** To describe the incidence of primary cutaneous squamous cell carcinoma in coastal NSW Australia.

**Methods:** The design is a case-controlled study of reported cSCC from 2016 to 2019 within a defined region of coastal southern NSW. Participants include all reported pathological diagnoses of cSCC in patients greater than 20 years of age. The main outcome measures the incidence and relative risk of cSCC.

**Results:** The age-adjusted incidence rate of primary cSCC was 856/10<sup>5</sup>/year. Men over 60 years of age had an age-adjusted incidence rate of 2875/10<sup>6</sup>/year. Histologically diagnosed invasive SCC samples were included using SNOMED clinical term codes. Keratoacanthomas and SCC *in situ* SNOMED codes were not included. SCC *in situ* results was found within the sample analysis and was offset by including one SCC *per annum* per person.

**Conclusions:** The rates of cSCC are far higher than previously reported and demand a reappraisal of our national management of this disease.

**Key words:** Australia, epidemiology, incidence, skin cancer, squamous cell carcinoma.

## Learning points

- There is no accurate data on cSCC incidence in mainland Australia
- The incidence of cSCC in mainland Australia is probably greater than appreciated
- With an ageing population, more accurate collection of data for cSCC is warranted

## INTRODUCTION

Australia has the highest incidence of skin cancer.<sup>1</sup> Squamous cell carcinoma (cSCC) and basal cell carcinoma (BCC) make up the most commonly diagnosed forms of keratinocyte cancer (KC), yet the data are captured by few cancer registries anywhere in the world. It is estimated that worldwide, the incidence of KC is greater than all other cancers combined. No mainland Australian cancer registry collects data for primary KC. As part of a comprehensive cancer registry, Tasmania, Australia has maintained a registry of KC for more than 40 years. Ragaini and colleagues recently published Tasmanian age-adjusted rates of cSCC of up to 514/10<sup>5</sup>/year.<sup>2</sup> The application of Tasmanian data to mainland Australia is problematic given the latitude differences nationally. The most recent mainland Australian KC incidence estimate was in 2002.<sup>3</sup> An analysis of Medicare data<sup>4</sup> showed that the highest incidence of billed treatment cSCC was estimated at 573/10<sup>5</sup> person-years in men in Queensland. The national incidence was estimated in 2002 at 499/10<sup>5</sup> for men and 291/

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$10^5$  for women.<sup>5</sup> It is likely that the true age-specific incidence of cSCC is grossly underestimated due to the absence of routine collection.<sup>5</sup> Unlike BCC, cSCC has a well-established capacity to metastasise. Metastatic cSCC has a poor 5-year survival.<sup>6,7</sup> Techniques to identify molecular biomarkers of metastasis and progression are the subject of current research.<sup>6</sup>

Accumulation of UV-induced skin somatic mutations and relative immunodeficiency with increasing age are likely to both play a role in this increased risk.<sup>6</sup> Fifteen percent of Australia's population in 2017 were aged 65 years and older. For those aged 65 have a longer life expectancy of 19.6 years for men and 22.3 years for women.<sup>7</sup> The ageing population also has an increasing burden of comorbidities making overall care more expensive and complex. It is well-known that Australians in regional to remote areas have less access to health services.<sup>8</sup> Immunosuppressed individuals develop cSCC more than 60 times that of their immunocompetent counterparts.<sup>9</sup> The cost of Medicare benefit claims paid for KC was \$127 million in 2014 and is predicted to rise by 39% every 10 years. More cases of KC were diagnosed in 2002 than all other cancers combined, and the predicted mortality rate is 1.9 deaths per 100 000 people.<sup>5</sup> This study aims to identify the incidence of primary cSCC in a well-defined geographic region of mainland Australia. A more accurate appreciation of the incidence of cSCC will allow for future proportionate health resource planning and skin cancer prevention.

## MATERIALS AND METHODS

To understand and accurately estimate the incidence of cSCC, data were collected from the major public and private histopathology laboratories in the Illawarra, Shoalhaven, Southern Highlands and Eurobodalla regions. This area relies on Southern IML, Laverty Pathology and NSW Health Pathology for the majority of histopathology. These laboratories were identified after a survey of medical practices providing primary skin cancer care. This survey included responses from general practitioners, skin cancer clinics, specialist dermatologists and surgeons involved in managing skin malignancy.

The unidentified data collected were over a 4-year period from 2016 to 2019. Each laboratory provided data for samples from the period with age, sex, postcode and primary cSCC diagnosis. Histologically diagnosed invasive SCC samples were included using SNOMED clinical term codes. Keratoacanthomas and SCC *in situ* SNOMED codes were not included. Each patient was counted only once per year, regardless of the number of cSCC they had diagnosed. This was to ensure that the same lesion could not be counted twice by being biopsied and then excised. A 5% audit of cases was completed to ensure the accuracy of the diagnosis reported.

Data were then combined with data from the 2016 Australian Census<sup>10</sup> to establish age- and sex-adjusted incidence within the geographical regions studied.

The relative risks of cSCC were calculated for each postcode weight. The binary outcome variable was suffering

from a cSCC or not. Patients were subdivided into three age-specific groups: <40, 40–59 and >60. Population data from the 2016 Australian Bureau of Statistics (ABS) Census data were used as the reference population for each postcode to scale each of the relative risk values per postcode population density.<sup>10</sup> These data provide a subregional analysis of incidence between- and within-age groups.

## RESULTS

ABS data showed a population > 20 years of age for the postcodes included in 2016 of 342 247.<sup>10</sup> Illawarra residents made up 74.3% of the population studied (Table 1). The average age in years for men was 74.3 and 75.8 for women with a cSCC diagnosis in the Illawarra Shoalhaven region from 2016 to 2019 (Table 2). Men represented 62.2% (7286/11 712 cases), a larger reported number of cSCC diagnoses in the region, compared with women 37.8% (4426/11 712 cases) (Table 3). The patients were divided into groups by age (20–39, 40–59, >60 years). The greatest numbers of the populace were > 60 years ( $n = 120\ 869$ ), followed by those 20–39 years ( $n = 110\ 855$ ) and those 40–59 years ( $n = 110\ 525$ ). The greatest difference in numbers by sex was in those >60 years where women made up 53.22%. The proportion was even greater for the Illawarra where the proportion was 53.34%.

The total number of primary cSCC reported across the entire region during the 4-year study period was 11 712, with an average annual number of 2928. The annualised incidence rate for the population over 20 years was 856/10<sup>5</sup>/year. After standardisation to national census data from 2016,<sup>10</sup> the age-adjusted annual incidence rate of cSCC was 777.3/10<sup>5</sup>/year for the population > 20 years of age.

The greatest rate was for men >60 years with an incidence of 2875/10<sup>5</sup>/year. For women >60 years, the incidence was 1530/10<sup>5</sup>/year. Men were diagnosed with cSCC 1.64 times as often as women. The overall incidence for those over 60 years was 2160/10<sup>5</sup>/year.

Older patients with a higher risk of cSCC tend to reside more coastally, whereas the opposite phenomenon is seen in younger populations at greater risk (Tables S1–S5). Younger populations who are at increased relative risk tend to reside more inland in the studied postcode areas (Fig. S1a–c).

## DISCUSSION

The challenges of collecting and analysing data for cSCC are well-known. In Australia, a 2014 parliamentary inquiry into keratinocyte cancer identified four options for better understanding the burden of KC.<sup>11</sup> These options: (i) include common KC as notifiable cancer in each state and territory, and collect complete data through cancer registries, (ii) include common KC as a notifiable cancer in selected regions of Australia and collect complete data for these regions through cancer registries, (iii) collect information through regular national surveys every 5 years, and (iv) investigate the utility of other available data for producing KC incidence estimates that are fit for purpose.

**Table 1** Incidence of cutaneous squamous cell carcinoma per 100 000 person-years in the Illawarra Shoalhaven Region 2016–2019

Age group (years) <sup>†</sup>	Population ( <i>n</i> ) <sup>‡</sup>			Cases ( <i>n</i> )	Cases/year ( <i>n</i> )	Rate <sup>§</sup>
	Illawarra	Shoalhaven	Total			
<b>Men</b>						
20–39	43 645	12 894	56 539	24	6	11
40–60	38 405	15 857	54 242	756	189	348
>60	34 381	22 167	56 548	6505	1626	2875
<b>Women</b>						
20–39	42 059	12 255	54 314	9	2	4
40–60	39 956	16 347	56 285	480	120	215
>60	39 308	25 013	64 321	3935	984	1530
<b>All</b>						
20–39	85 704	25 149	110 853	33	8	7
40–60	78 341	32 184	110 525	1236	309	280
>60	73 689	47 180	120 869	10 445	2611	2160
Totals	237 734	104 513	342 247	11 712	2928	856

cSCC, cutaneous squamous cell carcinoma.

<sup>†</sup>Gender.

<sup>‡</sup>Population age distribution of Illawarra and Shoalhaven Local Health Districts from the 2016 ABS Census data.<sup>10</sup>

<sup>§</sup>Age-adjusted and gender-adjusted incidence rate per 100 000 person-years.

**Table 2** Study region age in years for cSCC diagnosis 2016–2019

	Age (years)
<b>Mean</b>	
Male	74.3
Female	75.8
<b>Median</b>	
Male	75
Female	77
<b>Standard deviation</b>	
Male	10.7
Female	11.3
<b>Minimum</b>	
Male	28
Female	28
<b>Maximum</b>	
Male	101
Female	105

**Table 3** Study region gender for cSCC diagnosis 2016–2019

Gender	Counts ( <i>n</i> )	% of total	Cumulative %
Male	7286	62.2	62.2
Female	4426	37.8	100.0

The impetus for this parliamentary inquiry was the historical survey data we have cited in this report. The results of our study lend a new priority to this dilemma and ought to prompt a rethink of the national and international approach to understanding cSCC incidence.

Presented herein is the most detailed analysis of the incidence of primary cSCC within a region of southern NSW. The area from Helensburgh south to Moruya including the adjacent inland regions is largely serviced by a small number of histopathology laboratories. This geographic and medical services combination allowed for a relatively controlled audit of cSCC over a 4-year period from 2016 to 2019 matched to population data from the Australian Bureau of Statistics.

The incidence of primary cSCC in coastal southern NSW is extremely high. The highest incidence was for males over 60 years at 2875/10<sup>5</sup>/year. Females over 60 years had an incidence of 1530/10<sup>5</sup>/year. These rates of cSCC are more than four times greater than previously published data, whether registry-based, from surveys and by Medicare billing as a method for estimating incidence.<sup>2,5</sup>

Males were more 62.2% more likely to develop primary cSCC as females across all age groups. This sex disparity has long been thought to reflect both leisure and work habits of men favouring prolonged UV exposure throughout early life. It may be that there are molecular influences determining some of this observed difference.<sup>12</sup>

The relative risk of developing a primary cSCC was greatest in the southern and coastal regions of the study area for those over 60 years of age. This was not the case for those 40–60 years, where further inland saw the greatest relative risk. This analysis over larger areas would offer detailed information for education, early intervention and targeted surveillance in cSCC.

Comparing our data to that of Ragaini and colleagues from Tasmania, we found ethnographic and population similarities. In 2016, the Tasmanian population over 20 years of age was 330 657. Our study population over 20 years of age for the Illawarra and Shoalhaven regions was 342 247. The Tasmanian population greater than 60 years was 133 520 compared with 120 869 in the Illawarra Shoalhaven. More than 80% of the population of both regions was born in Australia, compared with 67% nationally. In Tasmania, households where a language other than English is spoken is 6.5%, whilst in the Illawarra and Shoalhaven, this is 14.4%. This compares to the national figure of 22%. However, for all these similarities, the effect of reduced distance from the equator is substantial when comparing cSCC incidence. The overall incidence for those over 60 years in our study was 2160/10<sup>5</sup>/year compared with a peak age-adjusted incidence of 514/10<sup>5</sup>/year in Tasmania.

All the limitations described herein would increase the incidence of cSCC reported. Firstly, there may have been cSCC not submitted for histopathologic assessment. This may have been in the circumstance of multiple lesions being treated and therefore not all submitted, or because the lesions were treated with destruction rather than biopsy or excision. Secondly, treated cSCC may have been submitted to histopathology providers not included in our data collection. Without routine notification of cSCC to cancer registries, a comprehensive collection of data is impossible. Thirdly, we have specifically excluded lesions reported for an individual after the first such diagnosis *per annum*.

Although a strength of the study, the use of postcode as the spatial unit to characterise area-level risk was also a limitation. The size of the spatial units used in cancer public health is limited due to patient privacy. This means that more nuanced analysis using parameters such as the SEIFA scores is not available. For larger geographies, such as postcodes, risk values are derived from the population-weighted average of smaller unit scores, which may mask socioeconomic diversity within an area. The use of larger spatial units such as postcode level information from public health registries such as the SEIFA information as a proxy for the socioeconomic disadvantage of individuals is susceptible to ecological inference fallacy, particularly whether there is individual diversity within the area. Although limitations of postcode level data need to be recognised in examining the relative risk of cSCC, cancer registries are subject to strict privacy policies. Notwithstanding, the results provided by this study are the finest dimension of analysis possible in oncological statistics and have been generated from a robust data source that has the potential for informing the targeting of broader scale community awareness initiatives.

This study provides our best estimate of the true incidence of primary cSCC in mainland Australia. It identifies a rate far in excess of that previously published or understood. It also highlights the challenges in *ad hoc* analysis of incidence in the absence of routine notification of cSCC. This study provides a platform for rediscussing the wisdom of excluding keratinocyte cancer from mainland state cancer registries. We propose that a method and agency for collecting these data nationally would allow for the appropriate resourcing of efforts to both prevent and manage cSCC in our communities.

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## Supporting Information

Additional Supporting Information may be found online in Supporting Information:

**Table S1.** Number of cSCC cases per age range for the Illawarra Shoalhaven region.

**Table S2.** Number of cSCC cases per gender per postcode in the Illawarra Shoalhaven Region.

**Table S3.** Postcode frequency for cSCC diagnosis 2016–2019.

**Figure S1.** a: Relative Risk of Cutaneous Squamous Cell Carcinoma for those under 40 years of age per 100 000 person years in the Illawarra Shoalhaven Region 2016–2019. b: Relative Risk of Cutaneous Squamous Cell Carcinoma for those aged between 40 to 60 years of age per 100 000 person years in the Illawarra Shoalhaven Region 2016–2019. c: Relative Risk of Cutaneous Squamous Cell Carcinoma for those over 60 years of age per 100 000 person years in the Illawarra Shoalhaven Region 2016–2019.