Received: 24 December 2022 | Accepted: 24 February 2023

DOI: 10.1111/jop.13421

ORIGINAL ARTICLE

Journal of Oral Pathology & Medicine WILEY

Oral cancer in Australia: Rising incidence and worsening mortality

Aria Sun[1] | Dileep Sharma[2,3] | Siu-Wai Choi[1] | Poornima Ramamurthy[2] | Peter Thomson[2]

[1]Oral & Maxillofacial Surgery, Faculty of Dentistry, The University of Hong Kong, Hong Kong, China

[2]College of Medicine and Dentistry, James Cook University, Cairns, Queensland, Australia

[3]Oral Health, School of Health Sciences, University of Newcastle, Callaghan, New South Wales, Australia

Correspondence
Peter Thomson, College of Medicine and Dentistry, James Cook University, Cairns, QLD, Australia.
Email: peter.thomson1@jcu.edu.au

Abstract

Background: Oral cancer, predominantly squamous cell carcinoma (SCC), is a lethal and deforming disease of rising incidence. Although largely preventable by eliminating harmful tobacco and alcohol risk factor behaviour, 5-year survival rates remain around 50%, primarily due to late presentation of advanced stage disease. Whilst low socio-economic status, regional and remote location and indigenous status are associated with head and neck cancer in general, detailed incidence and demographic data for oral SCC in Australia are limited. This study aimed to characterise the Queensland population at risk of oral SCC development.

Methods: Following ethical approval, the Queensland Cancer Register (QCR) dataset was analysed to determine patterns of incidence, anonymised patient demographics, clinical presentation and outcome data for oral SCC cases diagnosed between 1982 and 2018.

Results: Data from 9887 patients were obtained. Mean age at diagnosis was 64.55 years, with a male-to-female ratio of 2.51:1; males were diagnosed at a younger age ($p < 0.001$). At study census date, 59% of patients had died, with females demonstrating longer mean survival ($p < 0.001$). Clinicopathological data confirmed that SCC most commonly arose from tongue sites (49%) and, whilst tumours were predominantly moderately differentiated in nature (63%), patients with poorly differentiated carcinomas exhibited shortest survival times ($p < 0.05$). Over the 36-year study period, the number of diagnoses increased 4.49-fold, whilst the number of deaths increased 19.14-fold.

Conclusion: Oral SCC poses a significant and growing healthcare problem in Queensland. In the absence of national screening, characterising the high-risk oral SCC population facilitates pragmatic opportunities to raise disease awareness, to deliver targeted screening and effective primary prevention strategies, and to provide early interventional treatment intervention to reduce disease mortality and morbidity.

KEYWORDS
oral squamous cell carcinoma, risk factors

1 | INTRODUCTION

Oral cancer, predominantly squamous cell carcinoma (SCC) arising from mouth lining, is a lethal and deforming disease of rising incidence and global significance. Although largely preventable by the elimination of harmful tobacco and alcohol risk factor behaviour, 5-year survival rates remain around 50%, primarily due to late presentation of advanced stage disease.[1] Although cancer accounts for 3 in every 10 deaths in Australia, and registration of newly diagnosed cancers is required by law for each state and territory, specific information on clinicopathological presentation and clinical outcome data for oral SCC remains limited in the contemporary literature.

Oral SCC data are often combined within the generic descriptor head and neck cancer in many databases. Calculated at 21.6 per 100 000 population for the 2012/2016 period, head and neck cancer comprises one of the 10 most common cancers for men and women in Australia. Data analyses may be misleading, however, due to confusion between malignant neoplasms of disparate aetiology and behaviour, such as SCC arising on the lip, within the oral cavity, the tonsil and oropharynx, and also nasopharyngeal, laryngeal and salivary gland cancers. Recent Australian studies, for example, have reported substantive reductions in lip cancer, probably due to improved ultraviolet radiation protection, whilst human papillomavirus (HPV)-related tonsillar and oropharyngeal SCCs have undergone significant increase.[2–4]

In general, Australian cancer statistics reveal considerable geographical disparities between regional or remote regions of the country and highly populated, inner-city areas. Remote regions exhibit higher age-standardised incidence and mortality rates for all cancers compared with major cities, with people living in the most socioeconomically disadvantaged exhibiting the highest incidence rates for upper aerodigestive tract cancer.[2,5]

A more thorough and comprehensive analysis of contemporary oral SCC data in Australia, especially in relation to stratifying population risk, appears long overdue. Situated in the North-East of the country, occupying an area of nearly 1 900 000 km^2 and a population exceeding 5 million, Queensland is the second largest and third-most populous state in Australia. Whilst major cities are concentrated in the South-East, vast rural and regional areas extend throughout northern, central and western areas. The Queensland Cancer Registry (QCR) is one of the country's largest population-based cancer registries and, excluding skin cancer, maintains a comprehensive register of cancer cases diagnosed in Queensland since 1982.

The aim of this study, therefore, was to utilise the QCR to undertake a detailed, retrospective review to characterise patient demographics, tumour details and clinical outcomes for oral SCC within the state of Queensland.

2 | MATERIALS AND METHODS

2.1 | Data retrieval

Following ethical approval, the QCR was accessed for the period 1982 (when data were first compiled) to 2018 (most recent available data). Utilising the International Classification of Diseases, 10th Revision (ICD-10), codes relating to C01 and C02 (tongue), C03 (gingiva), C04 (floor of mouth), C05 (palate), C06 (mouth, unspecified), C9 (tonsil), C10 (oropharynx) and C14 (ill-defined sites in lip, oral cavity and pharynx) were selected to identify site-specific malignant neoplasms confirmed histopathologically as SCC. Anonymised clinical information including patient age, sex, age at diagnosis and mortality outcomes was compiled and then analysed via a password-protected spreadsheet.

2.2 | Statistical analysis

Descriptive statistics were used to analyse patient and tumour data and reported as mean, standard deviation (SD), 95% confidence intervals (95% CI) and percentages. Based upon the study census date of 31 December 2018, overall survival analyses were performed by Cox regression, using patient death and interval between diagnosis and death as dependent variables, to estimate the hazard ratio (HR) for sex and tumour site on patient survival; males and tonsil site were used as references. Continuous data analyses between groups were investigated using *t*-tests or one-way analysis of variance (ANOVA) if there were more than two groups. SPSS for iOS, version 27.0 (IBM Corp.) was used to perform all statistical analyses.

3 | RESULTS

A total of 9887 patients with oral SCC (7071 males and 2816 females, with an M:F ratio of 2.51:1) were identified from the database, and their descriptive analyses are presented in Table 1. The mean age at diagnosis was 64.55 years (SD 11.76). Males were diagnosed at a younger age, with a mean of 63.01 years (SD 10.93) compared with 68.36 years (SD 12.80) for females ($p < 0.001$). At the time of data retrieval, 5859 patients (59.26%) had died.

The most frequently recorded tumour site was the tongue (4077 patients or 41.24%), followed by the palatine tonsillar region (2152; 21.77%) and then floor of mouth (1173; 11.86%), with the lowest frequency seen at labial commissure sites (17; 0.17%).

As displayed in Figure 1, both the number of OSCC diagnoses and the number of deaths increased during the years 1982–2018. Whilst the number of diagnoses increased 4.49-fold, with a particularly notable rise from 2006 onwards, the number of deaths increased 19.14-fold over the 36-year period. The mean patient age at diagnosis and the mean age at death, however, remained relatively constant over the study period, as shown in Figure 2.

Table 1 also shows that the mean survival time for patients was 4.43 years (SD 5.47), with females exhibiting a longer mean survival of 4.83 years (SD 5.79) compared with 4.27 years (SD 5.33) for males ($p < 0.001$). With regards tumour site, mean survival was shortest for oropharynx SCC at 2.45 years (SD 3.99) and longest for labial commissure at 7.22 years (SD 9.18).

TABLE 1 Patient sex, age at diagnosis and clinical outcome according to cancer site.

Cancer site	No. of patients	No. deceased (% of total)	Mean age in years at diagnosis + (SD)	Mean survival in years + (SD)
All sites (total)	9887	5859 (59.26%)	64.55 (11.76)	4.43 (5.47)
Male	7071	4137 (58.51%)	63.01 (10.93)	4.27 (5.33)
Female	2816	1722 (61.15%)	68.26 (12.80)	4.83 (5.79)
Tongue (total)	4077	2320 (56.90%)	64.51 (12.06)	4.49 (5.71)
Male	2859	1641 (57.40%)	63.11 (11.07)	4.21 (5.54)
Female	1218	679 (55.75%)	67.90 (13.58)	5.15 (6.05)
Tonsil (total)	2152	986 (45.82%)	62.05 (11.06)	4.33 (5.12)
Male	1742	772 (44.32%)	61.78 (10.77)	4.26 (4.94)
Female	410	214 (52.20%)	63.05 (12.04)	4.57 (5.73)
Floor of mouth (total)	1173	824 (70.25%)	63.20 (10.59)	5.41 (5.92)
Male	842	589 (69.95%)	61.52 (10.06)	5.15 (5.73)
Female	331	235 (71.00%)	67.40 (10.76)	6.05 (6.35)
Hard and soft palate (total)	639	495 (77.46%)	64.80 (10.92)	4.28 (4.84)
Male	447	352 (78.75%)	63.47 (9.96)	4.35 (4.86)
Female	192	143 (74.48%)	68.06 (12.42)	4.09 (4.80)
Gingiva (total)	548	324 (59.12%)	69.43 (12.33)	4.02 (5.07)
Male	322	188 (58.39%)	67.13 (11.96)	3.75 (5.02)
Female	226	136 (60.18%)	72.62 (12.18)	4.41 (5.13)
Oropharynx (total)	393	289 (73.54%)	63.71 (10.31)	2.45 (3.99)
Male	310	225 (72.58%)	62.85 (10.37)	2.44 (4.01)
Female	83	64 (77.11%)	66.73 (9.56)	2.47 (3.96)
Buccal mucosa and vestibule (total)	379	250 (65.96%)	71.82 (13.11)	4.39 (6.00)
Male	176	109 (61.93%)	68.55 (13.15)	4.36 (5.99)
Female	203	141 (69.46%)	74.35 (12.56)	4.42 (6.04)
Retromolar area (total)	353	244 (69.12%)	65.23 (10.89)	4.43 (4.97)
Male	252	174 (69.05%)	63.18 (9.80)	4.51 (4.98)
Female	101	70 (69.31%)	70.31 (11.85)	4.25 (4.99)
Mouth (total)	102	81 (79.41%)	68.05 (13.05)	4.02 (4.95)
Male	66	53 (80.30%)	66.49 (13.57)	4.14 (5.12)
Female	36	28 (77.78%)	71.00 (11.66)	3.78 (4.70)
Ill-defined/overlapping lesion of lip, oral cavity and pharynx (total)	54	34 (62.96%)	61.65 (10.05)	3.47 (4.03)
Male	43	26 (60.47%)	60.81 (9.98)	3.55 (4.16)
Female	11	8 (72.73%)	64.38 (10.47)	3.20 (3.82)
Labial commissure (total)	17	12 (70.59%)	68.25 (13.38)	7.22 (9.18)
Male	5	8 (66.67%)	63.88 (14.14)	8.55 (10.94)
Female	12	4 (80.00%)	77.00 (6.06)	4.54 (3.91)

In terms of histopathological diagnoses, 4889 tumours (49.45%) were graded as moderately differentiated, with a further 2392 (24.19%) either poorly differentiated or undifferentiated in nature; differentiation was unrecorded for 1465 cases (14.8%). These tumour differentiation characteristics are presented in Table 2 and compared with patient demographic, clinical outcome and anatomical site data. Irrespective of tumour site, and for the 8422 cases where differentiation was known, patients with poorly differentiated tumours displayed the shortest mean survival time of 3.93 years (SD 5.12), whilst those with well-differentiated tumours had the longest survival at 5.31 years (SD 6.04); $p < 0.05$. One-way ANOVA analysis confirmed statistically significant differences in patients' mean survival time between well, moderately and poorly differentiated tumours ($p < 0.05$).

Table 3 summarises Cox regression analyses investigating the effects of patient sex and primary tumour site on long-term survival.

FIGURE 1 Trends in number of cases and number of deaths during the 36-year period.

Using males as reference, sex did not appear to impact overall survival with an HR of 1.039 (0.981–1.100 95% CI); $p = 0.189$. Due to its better survival data, based upon time from diagnosis to death and numbers of people still alive at census, tonsil was chosen as the reference tumour site. Oropharynx SCC showed the highest HR, and thereby the poorest patient survival, at 2.537 (2.225–2.893 95% CI); $p < 0.001$. Cumulative survival curves, plotted in Figure 3, confirmed the notably worse prognosis for patients with oropharynx SCC compared with tonsillar SCC.

4 | DISCUSSION

4.1 | Patient demographics

This study utilised retrospective data from 9887 patients diagnosed with oral SCC in Queensland over a 36-year period. The characteristic oral cancer patient in this study was male and in the sixth decade of life. The male-to-female ratio was 2.51 to 1, with females diagnosed at an older age. Of particular concern is the 4.49-fold increase in oral SCC cases observed during the study period, especially the more recent increase in numbers post-2006, as shown in Figure 1. Whilst the demographic profiling and rising incidence are consistent with other oral SCC population studies, the precise causation remains unclear. Although genetic predisposition and exogenous carcinogenic influences vary between populations, tobacco and alcohol misuse, diet and nutritional deficiencies, low socio-economic status and HPV infection may be of most relevance and in need of further investigation in this particular population.[6]

4.2 | Tumour characteristics

Whilst the tongue, tonsillar region and floor of mouth accounted for 75% of oral tumours in the study, the palate (6.5%), gingiva (5.5%), oropharynx (4%), buccal mucosa and vestibule (3.8%) and retromolar regions (3.6%) were much less frequently involved. Use of the non-specific categories 'Mouth' or 'Ill-defined/Overlapping Lesion' appear unhelpful limitations of ICD-10 coding, but as they only account for 1.6% of tumours in the present study are unlikely to have adversely influenced data analyses.

Table 2 shows no significant relationships between tumour differentiation and patient age, number of deaths or anatomical site of origin, but identification of poorly differentiated SCC, which accounted for nearly 24% of tumours, resulted in a significantly worse mean survival time (3.93 years). In general, it is recognised that patients are at risk of higher death rates if presenting with poorly differentiated or undifferentiated oral SCC compared with well-differentiated tumours.[7] It is disappointing, however, that tumour differentiation

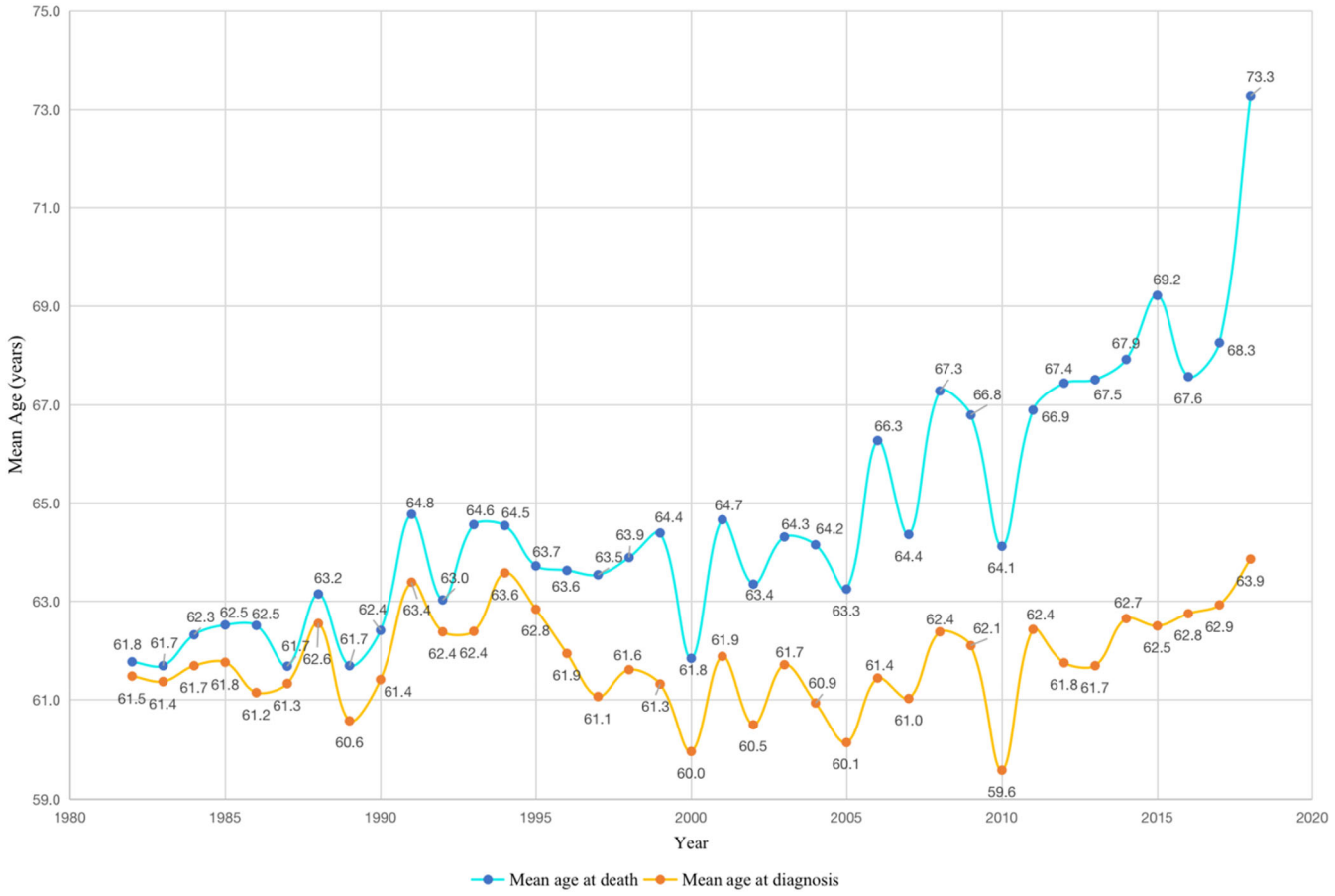

FIGURE 2 Trends in mean age at diagnosis and death during the 36-year period.

TABLE 2 Histopathological tumour differentiation characteristics.

	Well differentiated	Moderately differentiated	Poorly differentiated	Undifferentiated	Unknown
Total (all sites) (%)	1141 (11.54%)	4889 (49.45%)	2359 (23.86%)	33 (0.33%)	1465 (14.82%)
No. of deaths (%)	620 (54.34%)	3080 (63.00%)	1304 (55.28%)	23 (69.70%)	832 (56.79%)
Mean (SD) age at diagnosis	67.03 (12.12)	64.00 (11.54)	63.34 (11.31)	63.57 (13.34)	66.66 (22.41)
Mean (SD) survival (years)	5.31 (6.04)	4.78 (5.61)	3.93 (5.12)	4.45 (6.15)	3.29 (4.72)
Tongue (%)	527 (12.93%)	2005 (49.18%)	942 (23.11%)	10 (0.25%)	593 (14.55%)
Tonsil (%)	112 (5.20%)	874 (40.61%)	773 (35.92%)	14 (0.65%)	379 (17.61%)
Floor of mouth (%)	164 (13.98%)	692 (58.99%)	192 (16.37%)	3 (0.26%)	122 (10.40%)
Hard and soft palate (%)	79 (12.36%)	348 (54.46%)	115 (18.00%)	3 (0.47%)	94 (14.71%)
Gingiva (%)	104 (18.98%)	307 (56.02%)	83 (15.15%)	2 (0.36%)	52 (9.49%)
Oropharynx (%)	18 (4.58%)	186 (47.33%)	95 (24.17%)	-	94 (23.92%)
Buccal mucosa and vestibule (%)	76 (20.05%)	197 (51.98%)	56 (14.78%)	-	50 (13.19%)
Retromolar area (%)	38 (10.76%)	213 (60.34%)	69 (19.55%)	-	33 (9.35%)
Mouth (%)	15 (14.71%)	36 (35.29%)	16 (15.59%)	1 (0.98%)	34 (33.33%)
Ill-defined/overlapping lesion of lip, oral cavity and pharynx (%)	3 (5.56%)	25 (46.30%)	15 (27.78%)	-	11 (20.37%)
Labial commissure (%)	5 (29.41%)	6 (35.29%)	3 (17.65%)	-	3 (17.65%)

TABLE 3 Cox regression analyses investigating effect of sex and cancer site on survival ($n = 9877$).

	Hazard ratio	95% confidence interval	*p* value
Sex	1.039	0.981–1.100	0.189
Primary tumour site			
Tonsil	1.000	Reference	<0.001
Tongue	1.234	1.145–1.330	<0.001
Floor of mouth	1.404	1.280–1.541	<0.001
Hard and soft palate	1.836	1.648–2.046	<0.001
Gingiva	1.364	1.202–1.547	<0.001
Oropharynx	2.537	2.225–2.893	<0.001
Buccal mucosa and vestibule	1.562	1.357–1.797	<0.001
Retromolar area	1.622	1.410–1.867	<0.001
Mouth	1.908	1.521–2.393	<0.001
Ill-defined/overlapping lesion of lip, oral cavity and pharynx	1.726	1.226–2.430	0.002
Labial commissure	1.239	0.701–2.191	0.461

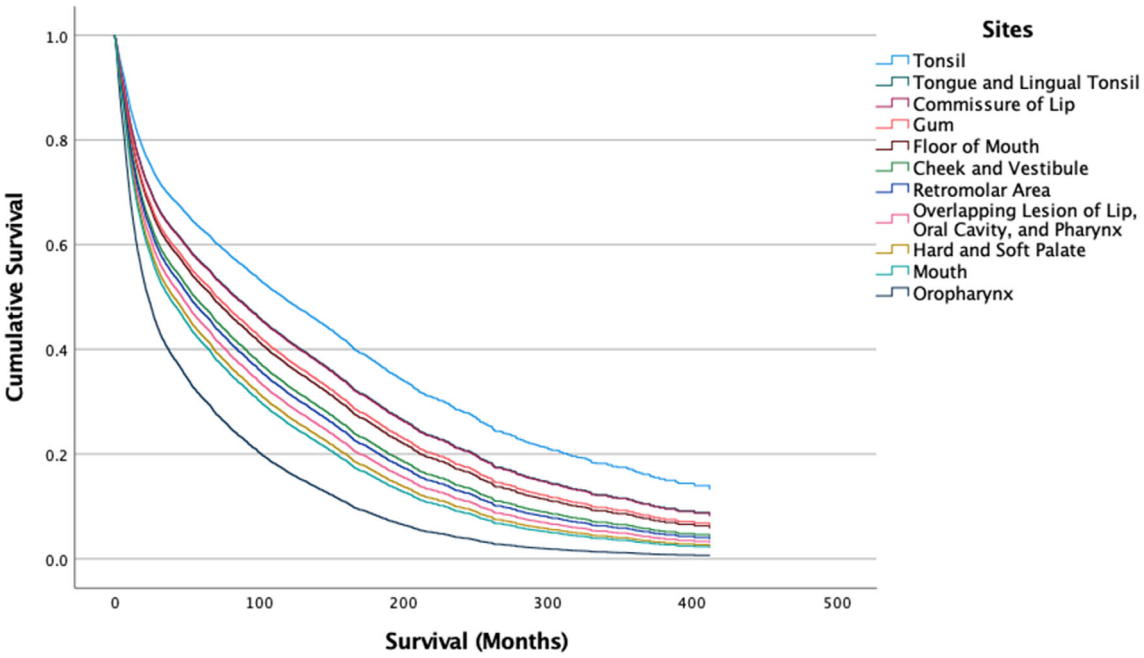

FIGURE 3 Cumulative survival versus primary tumour sites.

data were unrecorded for 15% of cases, as the significance of the shorter survival time (3.29 years) for this cohort remains uncertain.

4.3 | Clinical outcome

It is notable that 59% of the study population were deceased at the study census date, although this is based on overall patient survival because precise cause of death was not consistently available in the data set. Whilst the mean age at death remained consistent, there was a concerning 19.14-fold increase in deaths during the 36-year study period. Further research is ongoing to explore potential reasons behind this alarming observation.

Table 1 lists site-specific variation in mean survival times, with shortest survival noted for oropharynx (2.45 years); this is confirmed by HR 2.537 in Table 3 and by the cumulative survival curve in Figure 3. Oral SCC survival rates are known to be dependent upon tumour location and, although comprehensive treatment data are not recorded in the QCR database, poor 5-year survival has been previously reported for oropharynx SCC, probably due to late recognition

of poorly accessible, late-stage disease. Whilst HPV infection is now identified as an important aetiological factor in oropharyngeal SCC development, and may alter treatment strategies, HPV status was not routinely documented in the database.[8]

4.4 | Implications for clinical practice

It is well recognised that early diagnosis of oral SCC improves clinical outcomes and long-term patient survival, especially by identification and eradication of potentially malignant disease preceding invasive SCC. General population screening programmes are problematic due to limited public awareness of oral cancer and the fact that 'most at risk' individuals rarely attend for examination. As there are no oral cancer screening programmes in Australia, our ability to profile the contemporary oral SCC population and, where possible, stratify patient risk offers pragmatic opportunities to identify and then target groups deemed at particular risk of SCC development.[9,10]

4.5 | Study limitations

As a retrospective database review, study data inevitably suffer from variability in quality, particularly over long periods of time. Missing socio-demographic features, inadequate risk factor identification, lack of histopathological classification, limited treatment information and incomplete clinical outcome data can all confound a thorough cohort analysis. Nonetheless, the data obtained from this large, 9887 oral SCC patient study deliver an important baseline profile of disease activity within Queensland.

5 | CONCLUSION

This study has demonstrated a rising incidence and a worsening mortality for oral cavity cancer in Queensland. These observations are concerning and require further investigation. Oral SCC clearly poses a significant health problem in Queensland. In the absence of a national screening programme, characterising the population most at risk of oral SCC development facilitates pragmatic opportunities to raise disease awareness, to deliver targeted screening, effect primary prevention strategies and provide low morbidity, early interventional treatment intervention. Future studies are now underway to delineate an accurate socio-demographic and geographic profile of the 'high-risk' oral SCC population in Queensland.

ACKNOWLEDGMENT

Open access publishing facilitated by James Cook University, as part of the Wiley - James Cook University agreement via the Council of Australian University Librarians.

CONFLICT OF INTEREST

Authors declare no conflict of interests.

PEER REVIEW

The peer review history for this article is available at https://publons.com/publon/10.1111/jop.13421.

DATA AVAILABILITY STATEMENT

All datasets analysed during the study are available from the corresponding author on reasonable request.

ETHICS STATEMENT

Approval to conduct this retrospective study was obtained from the James Cook University Human Research Ethics Committee (Reference number H8609) and further approval under the Public Health Act 2005 provided by Queensland Health. The dataset was received from the National Cancer Registry as a de-identified, password-protected spreadsheet and all data managed under the Australian Code for the Responsible Conduct of Research.

ORCID

Siu-Wai Choi https://orcid.org/0000-0002-8189-790X
Peter Thomson https://orcid.org/0000-0002-2007-7975

REFERENCES

1. Thomson P. *Oral Cancer: From Prevention to Intervention*. Cambridge Scholars Publishing; 2019.
2. Australian Institute of Health and Welfare. *Cancer in Australia 2019*. Cancer series no.119. Cat. no. CAN 123. AIHW; 2019.
3. Ariyawardana A, Johnson NW. Trends of lip, oral cavity and oropharyngeal cancers in Australia 1982–2008: overall good news but with rising rates in the oropharynx. *BMC Cancer*. 2013;13(333):1-10.
4. Pollaers K, Kujan O, Johnson NW, Farah CS. Oral and oropharyngeal cancer in Oceania: incidence, mortality, trends and gaps in public databases as presented to the Global Oral Cancer Forum. *Transl Res Oral Oncol*. 2017;2:1-8.
5. Ramamurthy P, Sharma D, Thomson PJ. Oral cancer in Australia: regional and remote perspectives. *Fac Dent J*. 2022;13:41-45.
6. Choi S-W, Thomson P. Increasing incidence of oral cancer in Hong Kong – who, where…and why? *J Oral Pathol Med*. 2019; 48:483-490.
7. Liu S-A, Wang C-C, Jiang R-S, Lee F-Y, Lin W-J, Lin J-C. Pathological features and their prognostic impacts on oral cavity cancer patients among different subsites – a singe institute's experience in Taiwan. *Sci Rep*. 2017;7:7451. doi:10.1038/s41598-017-08022-w
8. Jehn P, Dittmann J, Zimmerer R, et al. Survival rates according to tumour location in patients with surgically treated oral and oropharyngeal squamous cell carcinoma. *Anticancer Res*. 2019;39:2527-2533.
9. Thomson PJ. Potentially malignant disorders – the case for intervention. *J Oral Pathol Med*. 2017;46:883-887.
10. Thomson PJ, Goodson ML, Smith DR. Profiling cancer risk in oral potentially malignant disorders – a patient cohort study. *J Oral Pathol Med*. 2017;46:888-895.

How to cite this article: Sun A, Sharma D, Choi S-W, Ramamurthy P, Thomson P. Oral cancer in Australia: Rising incidence and worsening mortality. *J Oral Pathol Med*. 2023; 52(4):328-334. doi:10.1111/jop.13421