

# Trends and ethnic disparities in oral and oro-pharyngeal cancers in South Africa, 1992-2001

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## ABSTRACT

**Objective:** To describe trends in the epidemiology of oral and of oro-pharyngeal (OAP) cancers in South Africa for the latest period available.

**Methods:** Data were obtained from the South African pathology-based National Cancer Registry. All new cases of OAP cancers diagnosed and confirmed histologically from 1992 to 2001 are included for the ICD-10 sites C00 to C14, excluding those involving the major salivary glands (C07-C08) and the nasopharynx (C11). OAP cancer incidence is reported by demographics (gender, age, race/ethnicity) and the anatomical sites involved. The analysis on anatomical sites was restricted to squamous cell carcinomas.

**Results:** Overall, males had a much higher OAP cancer incidence rate (world age-standardised incidence rate [ASIR]= 7.01/100 000 per year) than females (ASIR=1.99). However, among Asian/Indian South Africans, OAP cancer incidence was higher among females (ASIR=4.60) than among males (ASIR=3.80). OAP cancer, excluding those involving the lip, was highest among Coloureds (ASIR=5.72) and lowest among Blacks (ASIR=3.16). OAP cancer incidence was stable overall, but incidence rates increased significantly among Coloured South Africans over the period under review ( $p \leq 0.05$ ). Cancer specifically involving the oro-pharyngeal was most common among Coloureds and showed an increasing trend during the period under review.

## ACRONYMS

ASIR:	Age-Standardised Incidence Rate
HPV:	Human Papillomavirus
NCR:	National Cancer Registry
OAP:	Oral and Pharyngeal
SNOMED:	Standard Nomenclature of Medicine
ICDO:	International Classification of Diseases for Oncology (ICD-10)

**Conclusions:** Variations in the incidence of OAP cancers by gender, race/ethnicity and anatomic site indicate a need for culturally-targeted reductions in major risk factors, including promoting tobacco cessation and prevention of risky alcohol use. The implications of the role of the human papillomavirus (HPV) in the prevention of squamous cell carcinomas involving the oro-pharyngeal in South Africa require further investigation.

**Key words:** oral and oro-pharyngeal cancer; epidemiology; tobacco; alcohol; inequalities; ethnic disparities; trends; HPV

## INTRODUCTION

Cancers of the oral cavity and the oro-pharyngeal (OAP cancer) are amongst the leading cancer types globally, with over 400 000 cases annually (excluding nasopharyngeal cancers), making this the sixth most common kind of cancer.<sup>1</sup> Although there are significant differences in geographical distributions,<sup>2</sup> upper aero-digestive tract malignancies – predominantly squamous cell carcinomas – are always amongst the top ten occurring cancers, as indeed applies in South Africa.<sup>3,4</sup> However, there are significant ethnic and gender differences in the incidence of these cancers in South Africa, with the lowest rates recorded among females and those previously classified as Black Africans.<sup>3</sup>

Tobacco, both smoked and smokeless, and excessive alcohol consumption are the most important established risk factors for squamous cell carcinomas involving the mouth, tongue, oro- and hypopharynx.<sup>1,5,6</sup> Other established risk factors for oral squamous cell carcinomas include tobacco chewing, snuff use and areca nut/betel quid chewing.<sup>5,6</sup> An important risk factor for squamous cell carcinomas in the mouth, but more so the oro-pharyngeal region, is unsafe sexual practices. This may be particularly relevant in South Africa, given the high incidence of HIV/AIDS,<sup>7</sup> and the fact that HIV infection may increase the risk of acquiring infections with new human papillomaviruses (HPV) and decrease

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the rate of HPV clearance in both women and men.<sup>8</sup> Having oral sex with multiple partners has been associated with increased exposure to infection with the so-called "high-risk" HPV, viz: those of high-oncogenic potential.<sup>9,10</sup> HIV infection also remains the most important risk factor for AIDS-defining cancers, particularly non-Hodgkin's lymphoma and Kaposi-sarcoma, involving any site in the body, including the upper aero-digestive tract.<sup>11</sup> Further suggested risk factors include dietary micronutrient deficiencies,<sup>12</sup> and poverty.<sup>1,5,9,12,13</sup> World-wide, these cancers display a strong socio-economic gradient.<sup>14</sup> Hence, understanding the ethnic disparities in the burden of these cancers is important when advocating that cancer control should be a priority in the broader agenda of reducing health inequities in South Africa. This is especially important because race/ethnicity has been identified as one of the most significant indicators of poverty in South Africa, given that 61% of the Black African population, 38% of the Coloured population, 5% of the Indian/Asian population, and only 1% of the White population are categorised as poor.<sup>15</sup>

An earlier report on the incidence of "oral cancer" in South Africa covered only a short period of four years (1988-1991) and the findings may have been limited by erratic reporting to the then newly established pathology-based National Cancer Registry (NCR).<sup>3</sup> The present study therefore sought to provide a more current overview of the basic epidemiology of OAP cancers in South Africa over a longer period, namely that from 1992 to 2001 – a period for which the NCR data have been made publicly available. This period also was a time of significant escalation of the HIV/AIDs epidemic and of concomitantly increasing knowledge of the importance of HPV. These years are also marked by the implementation of important tobacco control legislation in South Africa. This study provides an opportunity to explore trends in the incidence of OAP cancers by site (and thus to consider possible aetiological risk factors) and, therefore, could provide an important baseline for future evaluations of the impact of the current cancer control strategies on oral cancer frequency in the longer-term.

## METHODS

The National Cancer Registry in South Africa is a pathology-based registry established in 1986. It seeks to collect comprehensive data regarding all cases of pathologically confirmed cancer in the country and to provide, to the extent possible, incidence rates for the country.<sup>4</sup> The Registry receives pathol-

ogy reports from all the universities having a medical facility (academic/training hospital) and from about 70 public and private pathology laboratories located across the nine provinces in the country.<sup>4</sup> Only cases of primary invasive cancer diagnosed by histology, cytology or haematology are recorded. Doubtful, *in situ* or borderline cancers are excluded. Until 1998, the primary site of the cancer was coded according to the Standard Nomenclature of Medicine (SNOMED) system (this excluded sub-sites). The WHO International Classification of Diseases for Oncology (ICD-10) was used from 1999. The equivalent ICD-10 codes were applied retrospectively in this study, however, to all cancer cases recorded from 1992.

In order to make our data comparable to that of previously published studies, new cases of cancer diagnosed and confirmed histologically from 1992 to 2001 are included in the present study for the ICD-10 sites C00 to C14. Sites C07 and C08 (salivary gland tumours) and C11 (cancers involving the nasopharynx) are excluded because these are, biologically, fundamentally different diseases. A total of 16 844 acceptable registrations were received from the NCR for the period under review. The initial frequency distribution analysis includes all these records. However, a number of records had incomplete demographic information, and these were excluded from cross-tabulations between the demographic and OAP cancer variables. The cross-tabulations are therefore based on a sample of 15 013 cases which have complete data. In order to be able to associate specific cancer sites with potential risk factors, we limited site analysis to squamous cell carcinomas involving the mouth itself – viz: the oral cavity and anterior two-thirds of the tongue (C02-C06), the oro-pharyngeal, including tonsils and base of tongue (C01, C09-C10). Piriform sinus (C12), hypopharynx (C13), and other ill-defined sites (C14) were combined because of small numbers (C12-14). We present trends for squamous cell carcinoma of the lip (C00) separately, as the original dataset did not adequately differentiate those which involved the vermilion border from those which involved the oral mucosa; yet, the etiological risk factors for the two parts are different.

SPSS Version 17 was used for the statistical analysis which initially explored the frequency distribution of the demographic variables (gender, age, race group) and the OAP cancer variables (all types and all sites). Then, relationships between these demographic variables and OAP cancer variables were assessed. Age-standardised incidence rates

**Table 1:** Oral and oro-pharyngeal cancer: incident cases (1992-2001), standardised incidence rate and mean age at diagnosis by racial group and gender.

	Oral and pharyngeal cancer cases over 10 years (%)	Age-Standardised Rates (ASR)		Mean age at diagnosis (SD) <sup>a</sup>
		All cancer sites	Excludes lip	
<b>Racial/ethnic group</b>				
Asian/Indian	480 (2.8)	4.21	4.07	57.0 (11.6)
Black	8 927 (53.0)	3.27	3.16	56.7 (12.7)
Coloured	1 930 (11.5)	6.04	5.72	57.2 (11.7)
White	5 100 (30.3)	7.42	5.48	59.8 (13.2) <sup>b</sup>
Unknown	407 (2.4)			
<b>Gender</b>				
All male	12 324 (73.1)	7.01	6.31	57.4 (12.3)
All female	3 905 (23.2)	1.99	1.78	58.9 (14.2) <sup>b</sup>
Unknown	615 (3.7)			
<b>Total</b>	<b>16 844</b>	<b>4.53 / 100 000</b>	<b>3.98/100 000</b>	<b>57.8 (12.8)</b>

<sup>a</sup> SD = Standard deviation; <sup>b</sup> Significantly higher than comparison groups at p<0.01

**Table 2:** Age-standardised incidence rates (per 100 000 per annum) and incidence ratios by gender and age group within each population group for all oral and oro-pharyngeal cancers.

	Asian/Indian	Black	Coloured	White
	ASIR			
Female	4.60	1.74	2.70	4.15
Male	3.80	5.65	9.96	10.94
Ratio M: F	0.83	3.25	3.67	2.64
<45 years of age	0.55	0.45	0.76	1.68
≥45 years of age	3.66	2.82	5.28	5.74
Ratio ≥45: <45	6.66	6.27	6.95	3.42

were computed using the world standard population, adjusting for cases from an unknown population group. Differences in the mean age at diagnosis over the period under review were explored among the various ethnic groups using analysis of variance (ANOVA).

When the observed annual age-adjusted incidence rates were plotted on a graph and were connected, the resulting lines were irregular, partly because of sampling variability. To address these irregularities, a four-year ordinary moving, average-smoothing procedure was applied to the observed data to generate line graphs for trends in the incidence rate over time. However, in determining the significance of trends over time, the actual value of the age-adjusted incidence rate for each year was used. Trend tests were performed for the various demographic groups and anatomical sites (for squamous cell carcinomas only), and statistical significance was set at  $p \leq 0.05$ . The standardised beta-coefficients ( $\beta$ ) of the slope and p-values were based on linear regression of ASR over time, as previously described.<sup>16</sup>

## RESULTS

The estimated age-standardised incidence rate over the study period was 4.53 per 100 000 of the population. OAP cancers were most commonly diagnosed at the end of the sixth decade of life (population mean=57.8 yrs), but at a significantly older age among Whites (59.8 yrs) than among other ethnic/race groups (Table 1). There was a difference between the incidence rates of OAP

cancer by racial group, even when those involving the lip are excluded (Table 1). Except among the Asian/Indian population, the incidence rate of OAP cancers for males was substantially higher than that for females (Table 2). The overall female: male ratio of OAP cancer incidence was 1:3.5. The incidence of OAP cancers among those younger than 45 years was over-represented among the White population (Table 2).

White South Africans had the highest incidence rates of OAP cancers until the last part of the period under review, when the incidence rates among Coloured males surpassed those among White males (Figure 1). As displayed in Figures 1 and 2, only Coloured South African males ( $p$  for trend=0.05) and females ( $p$  for trend=0.01) experienced a statistically-significant increasing trend in OAP cancer incidence over the period under review. White females tended to show a decreasing trend ( $p$  for trend=0.06). No statistically-significant differences in cancer incidence were observed over time among the other demographic groups.

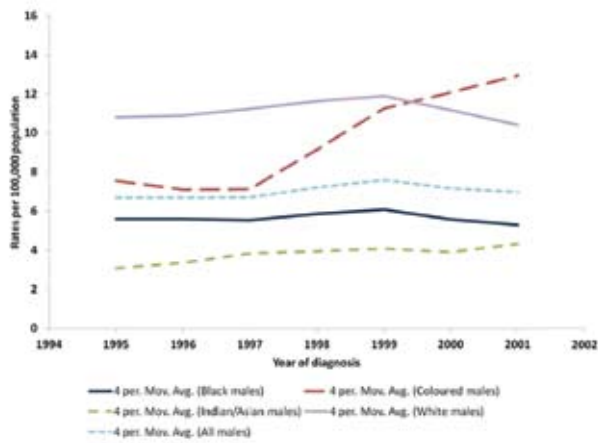
Of all OAP cancers, 89.4% ( $n=13,374$ ) were recorded as histological type squamous cell carcinoma. The incidence of squamous cell carcinoma involving the mouth itself was the highest and tended towards a decreasing trend after peaking in 1999 (Figure 3). Squamous cell carcinoma involving the oro-pharyngeal region was the only site that displayed an increasing, albeit non-statistically-significant, trend ( $\beta=0.58$ ;  $p=0.078$ ) over the whole period under review. However, the observed increase between 1995 and 2001 in the incidence of squamous cell carcinoma involving the oro-pharyngeal was statistically significant ( $\beta=0.78$ ;  $p$  for trend=0.045). Squamous cell carcinoma involving the lip (C00) was highest among Whites, but decreased significantly over the period under review ( $\beta=-0.78$ ;  $p$  for trend=0.008). Females and Asians/Indian tended to be over-represented among squamous cell carcinoma cases involving the mouth, while those younger than 45 years were over-represented among squamous cell carcinoma cases involving the oro-pharyngeal (Table 3).

## DISCUSSION

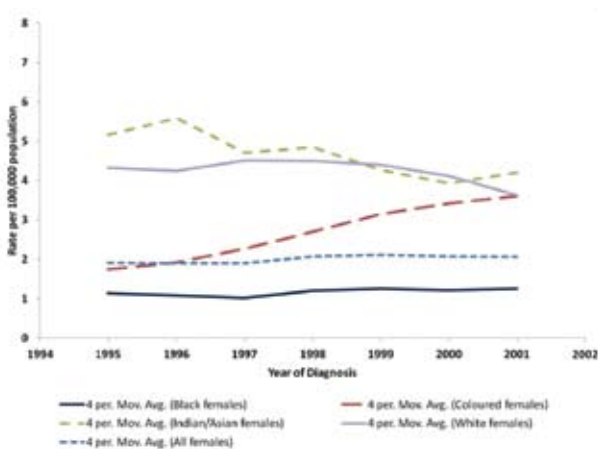
This study showed that, despite a stable incidence rate in the sample overall, those classified as Coloured South Af-

**Table 3:** Age-standardised incidence rates (per 100 000 per annum) of anatomical sites of oral and oro-pharyngeal squamous cell carcinomas by gender, age and racial/ethnic group.

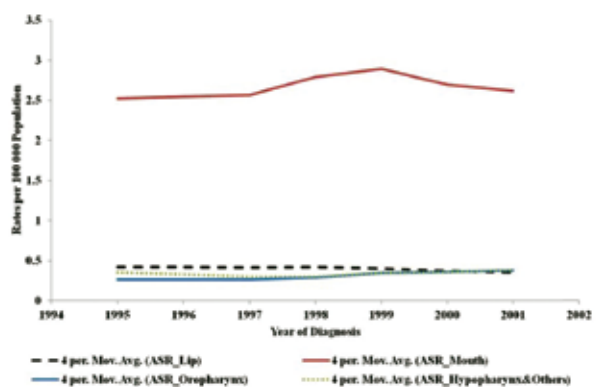
Demographics	Lip (C00)	Mouth (C02-C06)	Oro-pharyngeal (C01; C09-C10)	Hypopharynx & other ill-defined sites (C12-C14)	Total (Exclude lip)
Female (F)	0.18	1.21	0.11	0.15	1.47
Male (M)	0.65	4.27	0.56	0.69	5.52
Ratio M:F	3.44	3.53	5.09	4.60	3.76
< 45 years	0.08	0.32	0.04	0.04	0.40
≥45 years	0.32	2.33	0.26	0.36	2.95
Ratio ≥45:<45	4.00	7.28	6.50	9.00	7.38
Asian/Indian	0.09	2.81	0.18	0.46	3.45
Black	0.09	2.09	0.27	0.34	2.70
Coloured	0.29	4.10	0.59	0.73	5.42
White	1.87	4.20	0.46	0.48	5.14
Total popn	0.40	2.65	0.32	0.40	3.37



**Figure 1:** Trends in the age-standardised (world) oral and oro-pharyngeal cancer incidence rates among South African males by ethnicity/race, 1992-2001.



**Figure 2:** Trends in the age-standardised (world) oral and oro-pharyngeal cancer incidence rates among South African females by ethnicity/race, 1992-2001.



**Figure 3:** Trends in squamous cell carcinoma involving specific anatomical sites identified during the study period (1992-2001).

ricans displayed a statistically-significant increase in the incidence of oral and pharyngeal cancers during the period under review. The average overall incidence rates reported here are lower than the figures reported for the period from 1988 to 1991.<sup>3</sup> However, the oral and pharyngeal cancer rates observed in this study are of a magnitude similar to those more recently estimated among South Africans in general.<sup>17</sup> Therefore, oral and pharyngeal cancers continue to be a significant disease burden in South Africa, as is the case in many other countries in Africa.<sup>18-20</sup>

The finding that squamous cell carcinomas involving the lip were most common among Whites is consistent with the

literature.<sup>1</sup> This may be related to high smoking rates and/or low melanin skin pigmentation in Caucasians, considering that a significant proportion of these cancers are likely to involve the vermilion of the lip exposed to sunlight.<sup>3</sup> The decreasing trend in the incidence of lip cancers suggest that efforts directed over several years at preventing these cancers are bearing fruit. South African females, particularly those of Indian ancestry, were over-represented in squamous cell carcinoma cases involving the mouth. This may reflect the fact that, while smoking rates are generally low among South African women other than those classified as Coloureds,<sup>21</sup> the habit of chewing the highly carcinogenic areca nut with or without tobacco is more common among Indian females than among any other population group in South Africa.<sup>22</sup> Similarly, the oral application of smokeless tobacco (oral snuff) is more common among South African Black females, especially those of low socio-economic status,<sup>21</sup> than among other population groups.

The relatively low incidence rates of OAP cancers in general and squamous cell carcinomas in particular observed among Black South Africans could in part be related to under-reporting. Susceptible people in this population group are more likely to be those who are socio-economically disadvantaged and who reside in remote rural areas. Hence, reporting to a hospital facility for care is difficult, and consequently these patients are less likely to be included in this largely pathology-based cancer registry. However, it is also well known that one of the more common risk factors for squamous cell carcinoma of the upper aero-digestive tract, namely tobacco smoking, is less common among this population group.<sup>21</sup> Therefore, the implementation of culturally-sensitive programmes on the prevention of tobacco use among Black African men and women represents a window of opportunity to prevent a future increase in OAP cancers in South Africa.

It is pertinent to note that smoking prevalence among White South Africans (who had the highest incidence among the four racial/ethnic groups studied) was reported already to have started to decline in the 1980s. Among Coloureds, however, the prevalence of smoking has increased to levels similar to those reported for White South Africans.<sup>23,24</sup> Given that the OAP cancer incidence among those classified as Coloureds approached, or, in the case of males, even surpassed, that of White South Africans by the end of the period under review, it seems that the increasing trend in OAP squamous cell carcinoma incidence paralleled the increasing smoking rates about two decades prior to the cancer reporting period (a reasonable exposure period prior to cancer development). Among Coloureds, the rapid increase in OAP cancer incidence rates due to smoking may have been aggravated by simultaneous heavy alcohol use in segments of this population,<sup>25</sup> which, for decades, were known to have received part of their monthly wages in the form of alcoholic beverages, as part of the now abolished 'dop' system on the Cape wine farms.<sup>26</sup>

The incidence of squamous cell carcinoma involving the mouth appears to have stabilised. However, consistent with the literature,<sup>27</sup> cases of squamous cell carcinoma involving the oro- and hypopharynx show an increased trend over the period under review, despite the stabilisation of the aggregate cigarette consumption in the preceding 10 years.<sup>28</sup> This observation suggests that aetiological factors other than cigarette smoking may play a role in the



increased incidence of squamous cell carcinoma involving the oro-pharyngeal tissues. HPV has been suggested as an important oncogen for such cancers, especially among young adults.<sup>10,29</sup> The ethno-racial differences in incidence may be related to differences in the practice of oral sex.<sup>30</sup> The rate of clearance of HPV infection has been reported to be lower among smokers.<sup>31</sup> As Coloured South Africans had the highest incidence of squamous cell carcinoma involving the oro-pharyngeal region, that may then be explained in part by their relatively high rates of smoking. HPV-associated squamous cell carcinoma may be more prevalent among those with HIV infection.<sup>32</sup> Hence, the fact that the incidence of cancers involving the oro-pharyngeal tissues peaked and stabilised after 1999 may be related to the dramatic increase in HIV/AIDS-related mortality observed, particularly among those in their middle age.<sup>33</sup> The change in the recorded incidence of squamous cell carcinoma involving the oro-pharyngeal region may also be partly related to the change in disease classification codes used after 1998. Further studies are required to explore the role of HVP in upper aero-digestive tract cancers in South Africa in order to inform the design of appropriate prevention strategies.

OAP squamous cell carcinoma constituted about 90% of all OAP malignancies recorded in this study. Based on the current findings, and in accord with the literature, the pathways to the prevention of OAP squamous cell carcinoma appear to lie in encouraging the cessation of tobacco use among those who have already developed the habit, preventing the initiation of all forms of tobacco use among adolescents, and moderating alcohol use, especially among people of lower socio-economic status.<sup>34</sup> There needs to be an emphasis on sexual hygiene, especially amongst youth. Furthermore, as OAP cancers are relatively easily recognised, secondary prevention by opportunistic screening amongst high-risk groups would also have a valuable place in community control, and, notably, this does not require sophisticated special tests.<sup>35</sup>

#### Study limitations

Our data may not be truly representative of the situation in the country, as we have presented incidence rates from a pathology-based cancer registry, whereas a population-based cancer registry provides the best information on cancer incidence. However, the pathology-based NCR is the only comprehensive source of information on the burden of cancer in the country, and it is an advantage that the registry reflects national rates of histologically diagnosed cancers.<sup>4</sup>

A further limitation of our study is that we have had to present data without comprehensive analysis by histological type: notably we were unable to specifically identify cases of Kaposi's sarcoma (KS). Given the high prevalence of HIV/AIDS in South Africa,<sup>7</sup> and the continuing high incidence of KS in the immuno-suppressed, accurate data on KS are needed, both to help in controlling KS itself, and to avoid misinterpretation of the available data.<sup>36</sup> However, considering that 90% of the cancers reported are squamous cell carcinomata and that we have analysed these types separately, the information provided in this study remains useful for prioritising prevention strategies.

Clearly, the data presented in our study are dated. It is regrettable that data later than 2001 are not available.

However, considering that the equivalent aggregate incidence data on OAP cancers (including the lip) computed from the 2008 Globocan interactive database (ASIR=5.1)<sup>17</sup> is consistent with that presented in this study (ASIR=4.5), it is reasonable to assume that cancer incidence rates may not have changed significantly from those presented here.

The present study has, moreover, provided the added benefit of analysing cancer incidence among the various population groups, thus highlighting the ethnic distribution of the burden of oral and pharyngeal cancer in South Africa. Identifying the fact that Coloured South Africans have experienced an increase in OAP cancers, especially cancer of the oro-pharyngeal, will indeed help direct public health research to understanding how this might be explained – and prevented.

Whilst recognising then that the study has limitations, the present results should be useful in prioritising oral and pharyngeal cancer control strategies in South Africa. The findings highlight the need for culturally appropriate and targeted population interventions.

## CONCLUSIONS

The findings of this study suggest that the overall stable rates observed for oral and pharyngeal cancers over the study period may obscure important aspects of the underlying data. The data suggest, in fact, that while OAP squamous cell carcinoma rates are declining among Whites, they may simultaneously be increasing among minority ethnic groups, notably among people classified as Coloured South Africans. Our findings highlight the need for further studies to explore the reason(s) for what appears to be emerging differences in the trends in the anatomical location of OAP squamous cell carcinoma among South Africans over the period under review. In particular, the contributions of Kaposi's sarcoma, the role of HPV and the interaction of both Kaposi's sarcoma and HPV with the continuing HIV epidemic, and their implications for cancer prevention strategies in South Africa also require further investigation.

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