EPIDEMIOLOGY OF ORAL CANCER IN SOUTH AFRICA

1996-2002

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KEY WORDS

Mouth neoplasms

Oral cancer

Epidemiology

Incidence

South Africa

ABSTRACT

Background

Oral cancer is characterised by marked geographical differences in frequency and site preference as reported by various studies.

In South Africa, a few studies have been reported on the patterns and aetiology of oral cancer, and age standardised incidence rates (ASIR). Studies in several countries have shown an increase in oral cancer incidence among younger people.

Title: Epidemiology of oral cancer in South Africa 1996-2002.

Aim and Objective: The aim of this study was to determine the age standardised incidence rates (ASIR) of oral cancer by age, gender, race and site in South Africa for a consecutive period of seven years.

Method: Pathology case records of oral cancer diagnosed over a seven-year period from 1996 to 2002 and reported to the National Cancer Registry (NCR) were analysed for age, sex, race, and date of diagnosis, basis of diagnosis, topography and tumour type. The data was tabulated and categorised using Microsoft Excel. The South African population size for each year of the study was estimated by linear extrapolation using the 1996 and 2001 census results. Age standardisation incidence rates against the world population were calculated by the standard direct method.

Results: The total number of oral squamous cell carcinoma cases over the 7-year period was 9702. The majority of cases (34%) were on the tongue. The male to female ratio was 1:3. The age standardized incidence rates in this study was lower among African women; (0.640 per 100000 per year) and the highest was 13.40 new cases per 100000 per year (coloured males). Lip cancer was highest among both males and females of the white population. The cumulative rate of developing oral cancer was 1:83 and 1:32 for males and females respectively.

DECLARATION

I hereby declare that ***Epidemiology of Oral Cancer in South Africa 1996-2002*** is my own work, that it has not been submitted before for any degree or examination at any university,

and that all the sources I have used or quoted have been indicated and acknowledged by complete references.

MARY K. NDUI

Signed: 1st August 2011

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I would like to acknowledge the following people for their assistance in this research project:

Professor Hille J., my supervisor for his guidance and assistance in making this study possible.

The management of National Cancer Registry for providing the data on oral cancer and Dr. Theunis Kotze for his assistance with statistics.

DEDICATION

This work is dedicated to my loving husband David and our daughter Mercy for their endless support and encouragement during my study period.

Also to my loving sisters for their support and finally to the Kenyatta National Hospital management for giving me the opportunity to pursue this degree.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

CHAPTER 1

INTRODUCTION

Cancer is one of the most important medical problems in today's world. A great proportion of all deaths are related to cancer. The morbidity and prevalence of cancer makes it important in terms of general health, since a large amount of money is spent on this disease every year and the costs associated with the high number of lost human lives are incalculable. Oral cancer is among the ten most common cancers worldwide and ranks 4th in males. The incidence of oral cancer in South Africa was 3% of all diagnosed cancers in the period 1988-1995. The male to female ratio was 2.8:1 for all the population groups (Hille and Shear, 2001).

Epidemiological evidence shows that the incidence of head and neck cancer increases with age. In Europe, 98% of the patients diagnosed with this group of diseases are aged over 40 years. Although head and neck cancer rarely affects young patients, involving only 4% to 6% of persons aged below 40 years, reports indicate that this incidence has increased in a number of countries (Iamaroon *et al*., 2004). Diverse histological types of tumours are found in the oral region. Oral squamous cell carcinomas make up the vast majority of these cancers and arise from mucosal surfaces throughout this anatomic region (Ragin *et al*., 2007; Ologe *et al*., 2005). Oral cancer is strongly associated with certain environmental and lifestyle risk factors including tobacco, alcohol, and certain strains of the (mainly sexually transmitted) Human Papillomavirus. Data from Africa is however limited to a few hospital registries and it is therefore difficult to extrapolate the true incidence in these countries.

The purpose of this study is to obtain data on age standardised incidence rates of oral cancer in South Africa over the last seven years. It is also aimed at determining if there have been any changes in the trends of this cancer since the last reports.

CHAPTER 2

LITERATURE REVIEW

Introduction

Head and neck cancer (HNC) is a collective term based on anatomical and topographic definitions for describing malignant tumours arising from the mucosal surfaces of the upper aerodigestive tract, salivary glands, skin, gnathic and craniofacial bones, internal soft structures of head and neck including vessels, lymphoid structures, neural, adipose and connective tissues, and (neuro) endocrine tissues e.g. thyroid, parathyroid, etc (Davies and Welch, 2006). The most common histological type is squamous cell carcinoma which occurs in the oral cavity, oropharynx, hypopharynx and larynx and as metastatic tumours in the lymph nodes (Alvarenga *et al*., 2008; Vokes *et al*., 1993; Pai and Westra, 2009; Ragin *et al.*, 2007).

Epidemiology

The epidemiology of HNC receives limited attention in the general medical literature (Davies and Welch, 2006). Worldwide, an estimated 644,000 new cases of head and neck cancers are diagnosed each year, of which two-third occurs in developing countries (Marur and Forastiere, 2008).

In the United States, 45,600 new cases of head and neck squamous cell carcinoma were diagnosed in 2007, accounting for 3.2% of all incident malignancies and 2.2% (12,460) of all cancer deaths (Jemal *et al.,* 2005). Between 1973 and 1998, the incidence rate of oral cancer in the United States was reported to average 2.7 new cases per 100 000 population (Carvalho *et al.,* 2005). Men are affected three times more than women and the African Americans are affected more commonly than the white population (Marur and Forastiere, 2008; Hayat *et al*., 2007). In Kenya however, the incidence of oral cancer for the period of 1978-1997 was estimated at 2-3% of all malignancies (Onyango *et al*., 2004), which is the same as reported in the seventies (Onyango *et al*., 1980).

In the case of South Africa, several papers on age standardised incidence rate have been published. An age standardised incidence rate of 4.1 per 100 000 per year for African males and 1.5 per 100 000 per year for African females was reported between 1953 and 1955 (Oettle`, 1966, cited by Hille *et al*., 1996). Intra oral cancer in South Africa between 1988 and 1991, accounted for 5.0% and 1.8% of all cancers in males and females respectively. The

incidence rate among men and women in the different population groups respectively was 9.05 and 1.75 (black); 5.24 and 6.66 (Asian); 13.13 and 3.5 (coloured); and 8.06 and 3.18 (white). Asian women had the highest incidence among the females (Hille *et al.*, 1996). The age standardised incidence rate of oral cancer for the period 1993-1995 for males and females respectively in South Africa was 6.17 and 1.10 per 100 000 per year for blacks, 8.03 and 3.67 per 100 000 per year for whites, 4.49 and 8.88 per 100 000 per year for Asians and 8.85 and 1.94 per 100 000 per year for coloureds (Hille and Shear, 2001).

Among the Zimbabwean population, the age standardised incidence rate for oral cancer for the period of 1988-2000 for male and female was 1.09 and 0.51 per 100 000 per year with an average of 0.79 exclusive of lip cancer (Marimo and Hille, 2006). A Congolese study in the years 1958-1994, reported the incidence of oral squamous cell carcinoma as 2.1% of all cancers (Kayembe and Kalengayi, 1998). Incidence of oral cancer for 1988-1992 for males and females in Algeria was 1.1 and 0.3 and in Uganda during the same period was 1.2 and 1.9 per 100 000 per year (Franceschi *et al*., 2000).

Studies have shown marked differences in incidence of oral cancer by race. African American males have a higher incidence of oral and oropharyngeal cancers than Caucasian males – 20.7 versus 16.2 per 100 000 respectively, and the mortality rates being approximately twice as high as for white males (Murdock and Gluckman, 2001; Ries *et al*., 2005).

The five-year survival rate in United States is better for whites than for African-American patients. A study on cancer trends (Hayat *et al*., 2007) demonstrated the rates to be 61%-64% versus 40%-52%; and in another study 61.8% versus 39.5% (Ries *et al*., 2005). The worldwide five – year survival rate from oral cancer is generally less than 50%, with females tending to survive longer than males. These statistics remained unchanged for more than three decades (Ragin *et al*., 2007). Although there is a high cure rate for early oral cavity cancers, most patients present with advanced disease. The worldwide survival rate of oral cancer is among the lowest of the major cancers (Clayman *et al.,* 2003).

The incidence of oral cancer shows geographic and ethnic variations. According to the GLOBOCAN series of the International Agency for Research on Cancer (IARC), the estimated worldwide age standardized incidence for oral cavity cancer in the year 2002 were

6.3 per 100 000 for males and 3.2 per 100 000 for females (Parkin *et al*., 2005). Data from the GLOBOCAN program indicated that Asia had the highest number of cases of head and neck cancer for both males and females. The highest age standardised incidence rate (ASIR) of head and neck squamous cell carcinoma in 2002 among males was reported in Somme, France, ASIR of 46.2 per 100 000 and that of females 23.9 per 100000 in Pakistan. In 2002, the lowest rates for both males and females were reported from Valdivia, Chile (Hashibe *et al*., 2010). Varying incidence rates among different race/ethnic groups the between 1992 and 2004 were also reported by the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute (NIC). The rates for males versus females were as indicated; non Hispanic (7.1 vs 3.3), black (8.6 vs 2.7), American Indian (4.2 vs 2.4), Asian/Pacific Islander (3.6 vs 2.1) and Hispanic Latino (3.8 vs 1.8), (Brown *et al*., 2010). All rates were calculated per 100 000.

Risk factors

The aetiology of head and neck cancer is multifactorial with no single agent or factor being clearly defined as being causative for oral cancer. In an article on risk factors for oral cancer, the risks were classified as major risk factors, emerging risk factors, and cited controversial factors with no scientific evidences (Warnakulasuriya, 2009a).

<u>Major risk factors</u>

Tobacco and alcohol

Chronic tobacco smoking and alcohol consumption are well established life-style associated risk factors for the development of head and neck squamous cell carcinoma. Heavy tobacco users have a 5 to 25-fold higher risk of developing head and neck cancer than non-smokers (Goldenberg *et al*., 2004).

Oral cancer is the most common form of cancer in certain parts of Africa and Asia. The frequently aetiological factors associated are endemic tobacco smoking and chewing of tobacco and chewing betel quid (Hashibe *et al*., 2005). Descriptive studies from Sudan suggest that oral cancer rates in males are high, linking this to the high incidence of "Toombak" - a product of oral snuff mixed with sodium bicarbonate (Idris *et al*., 1995).

More so, numerous studies have shown that tobacco and alcohol use increases the risk of oral cancer in a dose response fashion and the joint effects are synergistic. Evidence associating a particular type of alcoholic drink with different effects on oral cancer is not clear (Murata *et al.,* 1996; Lewin *et al*., 1998; Talamini *et al*., 2002; Castellsague *et al*., 2004). In Spain, a study on alcohol and tobacco in oral carcinogenesis showed that all forms of tobacco increased the risk for oral cancer development. Smokers of black tobacco had a 3.3 fold increase in the risk of developing oral cancer than smokers of blond or mixed tobacco. Tobacco smoking only and alcohol consumption only was associated with a moderate increase in cancer risk. Tobacco smoking and use of alcohol simultaneously had a 13-fold increase in the risk of developing oral cancer (Castellsague *et al*., 2004). There are other cultural and habitual risk factors which predispose to the development of oral cancer. These include use of smokeless tobacco in the United States and Northern Europe, chewing the Betel-quid or Areca nut in India and some parts of Southeast Asia and South Africa. In Yemen and parts of the African continent, chewing of Khat is commonly practised (Goldenberg *et al*., 2004). Betel-quid is associated with the development of oral submucous fibrosis, a premalignant condition. Individuals affected by submucous fibrosis have a 19 fold higher risk of developing oral squamous cell carcinoma (Warnakulasuriya *et al*., 2002). In United States, African Americans have a higher incidence rate for tobacco related cancers than the white population (Johnson, 2001).

Human Papillomavirus

Accumulating evidence suggests that human papillomavirus (HPV) is a risk factor in the aetiology of head and neck cancers. The subtypes 6 and 16 are associated with increased risk in cancer of posterior tongue and tonsil (Schwartz *et al*., 1998). Epidemiological and molecular biology studies have suggested that HPV infection may be associated with 25% of all head and neck carcinomas and 60% of oropharyngeal carcinomas (McKaig *et al*., 1998; Gillison, 2004). The results of a case control study conducted by the International Agency for Research on Cancer point to a likely role of HPV in the aetiology of oropharyngeal and cancers of the oral cavity. Herrero *et al*. (2003) demonstrated that 3.9% of 766 oral cavity cancers and 18.3% of 142 oropharyngeal cancers tested positive for HPV DNA. The human papillomavirus related cancers were more frequent in the oropharynx and tonsil and also among non smokers than in smokers (Gillison, 2004; Herrero *et al.,* 2003). Conversely,

several studies reported varying frequencies of HPV involvement in oral cancer. These results may have been attributed to the population of study, type of specimen and the detection method applied (Shah, 1998; Mork *et al*., 2001).

Trauma

Chronic trauma of the oral mucosa, together with other factors, has been suggested to be an important risk factor in patients with oral cancer diagnosis. Piemonte *et al*. (2010) have reported an increased risk (OR=5.5) of developing oral cancer in the presence of longstanding oral mucosal trauma.

Emerging risk factors

Diet and nutrition

Dietary factors are important risk factors for oral and pharyngeal cancers. Several epidemiological studies have linked these cancers with vitamin A deficiency and with iron deficiency associated with the Plummer Vinson syndrome (Wahlberg *et al*., 1998). A meta-analysis on observational studies investigating the effects of fruit and vegetable consumption on oral cancer concluded that a daily portion of fruit and vegetables is associated with a significant reduction in the risk of oral cancer (Pavia *et al*., 2006). Consuming three or more portions of fruit and vegetable during childhood significantly reduces the risk of oral cancer compared to those consuming two portions or less and this may be an important factor in patients affected by cancer at a younger age (Llewellyn *et al*., 2004).

Immunosuppression

An increase in lip cancer has been reported in patients who have undergone renal transplantation and it was attributed to immunosuppression (King *et al*., 1995, Grulich *et al*., 2007). Lip cancer has also been shown to have a strong relationship with exposure to ultraviolet component of sunlight. This predominates in people with light complexion and those involved in outdoor occupation such as farmers and sailors (Neville *et al*., 2009).

Socio-economic status

Low socio-economic status in terms of low income, level of education and occupation class increased the risk for oral cancer across the world **(**Conway *et al.*, 2008).

Cited controversial factors with no scientific evidence

Human immunodeficiency virus (HIV) infection

Immunosuppression in HIV infection has been anticipated to increase the risk for oral cancer. Although HIV/AIDS is associated with a number of malignancies but the pandemic has not influenced the pattern of oral cancer in Kenya. The authors speculated that the HIV associated cases of oral squamous cell carcinoma had not risen to large numbers to influence the pattern of oral cancer in the country (Onyango *et al.*, 2004). This study did not indicate the frequency of the other categories of oral malignancies.

In Kenya, a study involving 200 HIV-infected patients showed that oral Kaposi's sarcoma accounted for 68%, squamous cell carcinoma 17%, non Hodgkin's lymphoma 13% and Burkitt's lymphoma 2% of head and neck neoplasms. Another finding was that the patients were affected by the malignancies at a younger age than in non-HIV infected population (Butt *et al.*, 2008). Based on studies done so far, there is no epidemiological evidence to proof association between HIV/AIDS and oral cancer (Shiboski *et al*., 2009).

Other cited factors

Other cited factors without scientific evidence are heredity and familial risk, marijuana smoking and alcohol in mouthwashes (Warnakulasuriya, 2009a).

Oral cancer in young people

Epidemiological evidence shows that the incidence of head and neck cancer increases with age. In Europe, 98% of the patients are aged over 40 years. It has been documented that this type of tumour is rare in young people, involving only 4% to 6% of persons aged below 40 years, although the incidence has increased in a number of countries (Iamaroon *et al*., 2004). Increase in the incidence of oral cancer in the young (less than 45 years) has been reported in the United States of America, England and Scotland (Robinson and Macfarlane, 2003; Llewellyn *et al*., 2003; Schantz and Yu, 2002). In Scotland, a 31% rise in the incidence of oral cancer in young people was reported between 1989 and 1996. Although majority of the

young people had a history of alcohol consumption and smoking, these risk factors did not appear to be important. The researchers concluded that other factors such as genetics might have played an important role in oral cancer in this group of patients (Robinson and Macfarlane, 2003). High incidence of oral cancer before the age of 35 years could be due to increased use of different forms of tobacco (Johnson, 2001).

A study to assess the changing trends in oral squamous carcinoma for the period 1971 to 2006 at Emory University, USA, reported that 5% of 1919 patients were less than 40 years old. There was a significant increase in number of cases reported in younger population from 1970s to 1980s (2.5–7.59%, p=0.003) and a plateau from 1990s to 2001 – 2006. The average age at presentation was 32.5 years and there was no difference between males and females. These results were contrary to those reported older individuals where females were approximately five years older than males (Müller *et al*., 2008). In addition, there was a notable increase in cancer of the mobile tongue among the young individuals compared to the older individuals. A 62% increase of head and neck cancer was reported in young American individuals when the periods 1973 – 1984 and 1985 – 1997 were compared (Schantz and Yu, 2002). The increase was in part attributed to the rise in tongue cancer. Similarly, a significant increase (62.1%) in the incidence of squamous cell carcinoma of the tongue was reported in the young cohort compared to 27.4% in those older than 40 years during 1990–2001 (Müller *et al*., 2008). The reason for the preference of squamous cell carcinoma for this site has not been elucidated.

The possibility of a genetic predisposition to oral cancer is suggested by its sporadic occurrence in young adults and in non-users of tobacco and alcohol. Occurrence of cancers at younger age is associated with hereditary factors (Lund and Howard, 1990; Hirota *et al*., 2008; Llewellyn *et al*., 2003).

Carcinogenesis

Many gene alterations have been implicated in the development and progression of oral squamous cell carcinoma. Tumour suppressor genes control cellular proliferation and a variety of other processes important for tissue homeostasis (Hollstein *et al*., 1994). p53 has been identified as an important tumour suppressor gene that repairs a potentially malignant cell or destroys it by apoptosis (Scully and Bagan, 2009). Anomalies of proto-oncogenes and

inactivation of tumour suppressor genes are involved in the multi step process of carcinogenesis. Loss of heterozygosity in the tumour suppressor genes is associated with the transformation of a normal cell to dysplastic one (Prime *et al*., 1997). A p53 mutation in tumours is associated with a poor prognosis and its detection may assist clinicians in treatment planning (Hollstein *et al*., 1994). An individual's genotype determines their immune response and this may influence in development of oral squamous cell carcinoma (Scully and Bagan, 2009).

Oncogenes play an important role in the initiation and progression of carcinogenesis (Neville *et al*., 2009). Epidermal growth factor receptor is over expressed in up to 80-90% of head and neck cancer. Elevated level of epidermal growth factor is a prognostic marker correlating with increased tumour size, increased risk of recurrence, and reduced response to radiation (Molinolo *et al*., 2009). Emerging information on the nature of mechanisms involved in progression of head and neck cancer could be translated into clinically relevant diagnostic and treatment modalities for the care of oral squamous cell carcinoma patients (Molinolo *et al*., 2009).

In conclusion, it is evident that the cause of oral squamous cell carcinoma is multifactorial and complex. Each of the individual factors reviewed above is not sufficient to cause cancer but are associated with an increased risk of the development of cancer. Socio-economic, cultural and geographic variables are possible confounding factors (Dobrossy, 2005).

CHAPTER 3

AIMS AND OBJECTIVES

Aims

This study aims at determining the incidence and pattern of distribution of oral cancer in South Africa over a period of 7 years, from 1996-2002.

Objectives

It is the purpose of this study to:

1. Determine the age standardised incidence rate (ASIR) of oral cancer by age, gender, race and site.
2. Determine the lifetime risk to develop oral cancer of the population under study.
3. Describe the incidence of cancers of the oral cavity and compare these to the previous studies.

HYPOTHESIS

The overall incidence of oral cancer has been rising in South Africa and increasingly affects the younger population.

CHAPTER 4

STUDY DESIGN AND METHODOLOGY

Study design

This was a retrospective descriptive study using routine data from the population based National Cancer Registry of South Africa during a period of 7 years.

Population/sample

This included all the patients in South Africa diagnosed with oral cancers from January 1996 to December 2002, a total of 9702 cases.

Data collection

Records of all cases of oral cancer from 1996 to 2002 were obtained from the National Cancer Registry (NCR), previously managed by the South African Medical Research Institute (SAMRI) until 2003 and now based at the National Hospital Laboratory Services (NHLS). The NCR is a passive pathology-based surveillance system and collects details of cases with histologically and/or cytologically confirmed cancer from copies of pathology reports confirming a cancer diagnosis which are submitted voluntary by all public and private pathology laboratories throughout South Africa (Sitas, 1995, cited by Hille *et al.*, 1996). The raw data for the reported cancer cases for the years 1996 to 2002 included those from the lip, mouth, tongue, gingiva, oropharynx, floor of mouth, tonsil, palate, nasopharynx, hypopharynx, salivary glands and pharynx.

These data had been digitalised using the CanReg version software, designed by the Unit of Descriptive Epidemiology of the IARC which includes the 'duplicate and person search' module for data validation and identification of duplicate entries. The information recorded on each case in the raw data included a registration number that identified the patient, the year of diagnosis, diagnosis date, age, sex, population group, incident date, morphology and topography of cancer and the International Classification of Diseases - 10 (ICD - 10) as shown in appendix I.

Data analysis

The anatomical sites (topography) included in this study were classified into 8 groups as follows:

Floor of mouth	Floor of mouth NOS, anterior floor of mouth
Tongue	Base of tongue NOS, tongue NOS, ventral surface of tongue NOS, border of tongue, anterior 2/3 of tongue NOS, dorsal surface of tongue NOS, lingual tonsil.
Lip	Lip NOS, mucosa of lower lip, external lip NOS, external lower lip, external upper lip
Gingiva	Gum NOS, lower gum, and upper gum
Palate	Palate NOS, soft palate NOS, hard palate, and uvula
Tonsil	Tonsil NOS, tonsillar fossa, and tonsillar pillar
Mouth	Mouth NOS, cheek mucosa, retromolar area, and vestibule
Oropharynx	Oropharynx NOS and vallecula

The gender was classified as males, females and unknown. The population groups were Asian, African, Coloured, White, and unknown while the age distribution was put in 5 – year groups from 0-4 to 85+ and “unknowns”.

The histomorphology was grouped into four categories. The group classified as squamous cell carcinoma was used for calculating the age standardised incidence rates. The other malignant neoplasms in the sites included in this study were grouped as carcinomas (other nonsquamous cell carcinomas), sarcomas and other malignancies.

The squamous cell carcinoma group included adenosquamous carcinoma, carcinoma NOS, carcinoma undifferentiated NOS, carcinoma anaplastic NOS, basaloid squamous cell carcinoma, large cell carcinoma NOS, papillary squamous cell carcinoma, spindle cell carcinoma NOS, squamous cell carcinoma with horn formation, squamous cell carcinoma adenoid, squamous cell carcinoma clear cell type, squamous cell carcinoma keratinizing

NOS, squamous cell carcinoma large cell non keratinizing NOS, squamous cell carcinoma microinvasive, squamous cell carcinoma NOS, squamous cell carcinoma small cell non-keratinizing, squamous cell carcinoma spindle cell, verrucous carcinoma, basaloid carcinoma and malignant neoplasm. The latter category was included in this group since the simplified NHLS SNOMED reporting codes are not specific for histological subtypes and most often the corresponding malignancies are squamous in nature.

Population data was derived from the corresponding National Census results published online (Statistics South Africa, 2004). The 1996 and 2001 population census data were used to calculate the weighted mean population size. The estimated population size for each population group per year was calculated by linear interpolation (appendix III). The population pyramid for the year 2000 was constructed in power point (Microsoft) using the extrapolated population data from the 1996 and 2001 census report (Statistics South Africa, 2004). The data were tabulated using an Excel (Microsoft ^{TM}) spreadsheet for each year, population group and gender. The crude rate, age specific morbidity rate, adjusted age specific incidence rate, cumulative rate and cumulative (lifetime) risk for oral cancer was calculated. Using the direct method described by the IARC (Waterhouse et al., 1976), the adjusted age specific incidence rates were standardized against world population and recorded as the incidence per 100 000 population per year; adjustments for unknown age was made.

Inclusion criteria

Records of cases from the anatomical sites selected for this study with a diagnosis of squamous cell carcinoma and the other diagnoses included in this group.

Exclusion criteria

Records of cases categorised as carcinomas, sarcomas and other malignancies.

CHAPTER 5

RESULTS

5.1 Frequency of new squamous cell carcinoma cases

In the period 1996 – 2002, there were 9702 new cases of oral squamous cell carcinoma involving all sites included in this study. There was slight annual variation in the frequency of new cases over the 7 years. The highest number of reported cases occurred during 1996 (15.2%), while the year 2000 recorded the lowest (11.5%). Consistent numbers of reported oral squamous cell carcinomas were reported between 1996 – 1998 and 2001 – 2002 (table 1 and figure 1).

	1996	1997	1998	1999	2000	2001	2002
Male	1159	1077	1069	1013	854	969	937
Female	318	324	350	325	257	295	325
Total	1477	1401	1419	1338	1111	1264	1262

Table 1. Frequency of oral and lip cancer cases recorded per year.

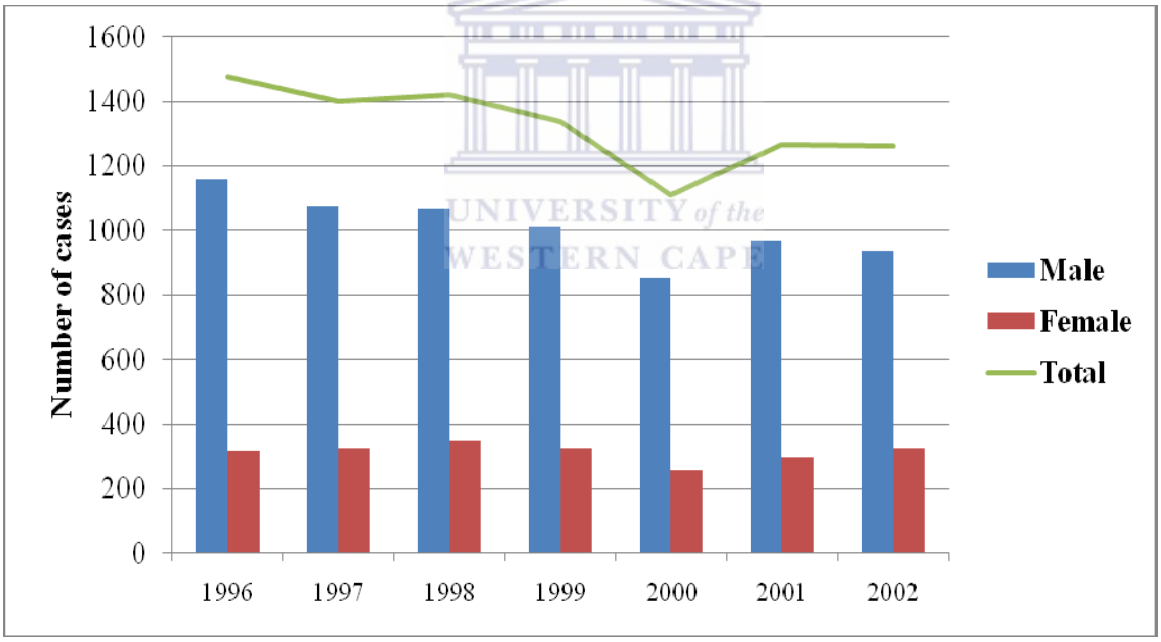

Figure 1. Bar graph showing annual distribution of oral and lip cancer for all population groups.

5.2 Gender distribution

The majority of oral squamous cell carcinoma cases diagnosed in the seven year period occurred in males except in the Asian population where the females were slightly more affected (figure 2). Among the males, the African population represented 3500 (59.5%) of the cases of oral cancer. The male to female ratio for all groups was 3:1, the Africans having a ratio of 4.5:1 (table 2).

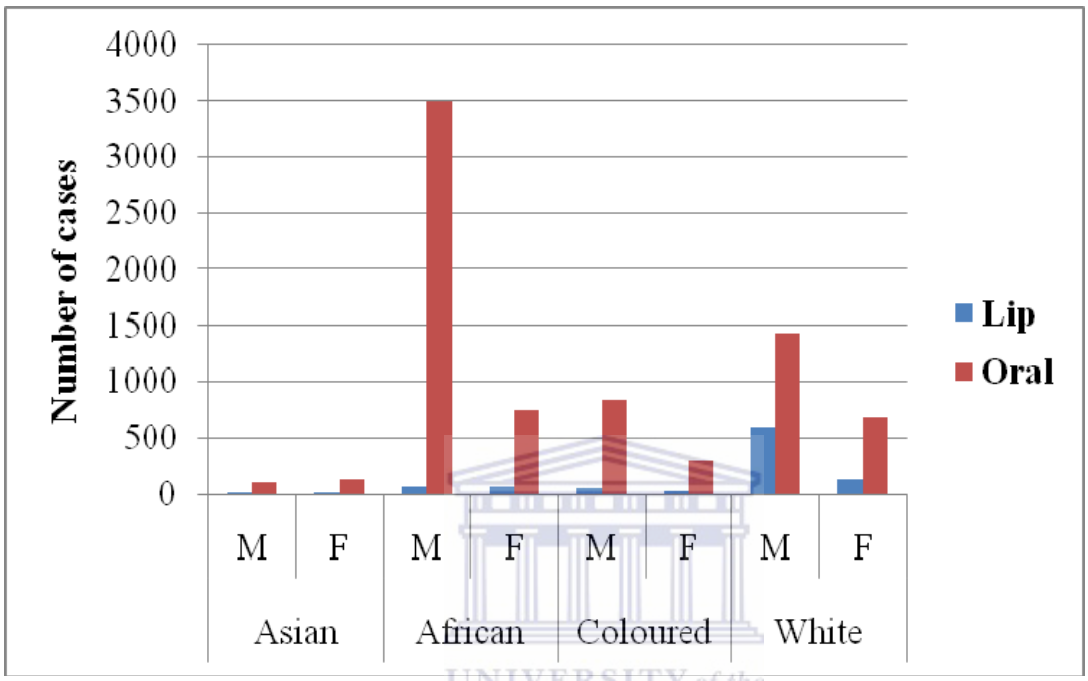

Figure 2. Bar graph showing oral and lip cancer distribution by gender and population group 1996 – 2002.

	Male		Female		Oral cancer Ratio M:F
	Oral	Lip	Oral	Lip	

African	3500	66	737	65	4.5:1
Coloured	840	54	290	28	2.8:1
White	1436	595	689	127	2.5:1
Asian	105	7	127	3	1:1.2
Total	5881	722	1843	233	3:1

Table 2. Frequency of oral and lip cancer and the gender ratio 1996 – 2002.

5.3 Age distribution

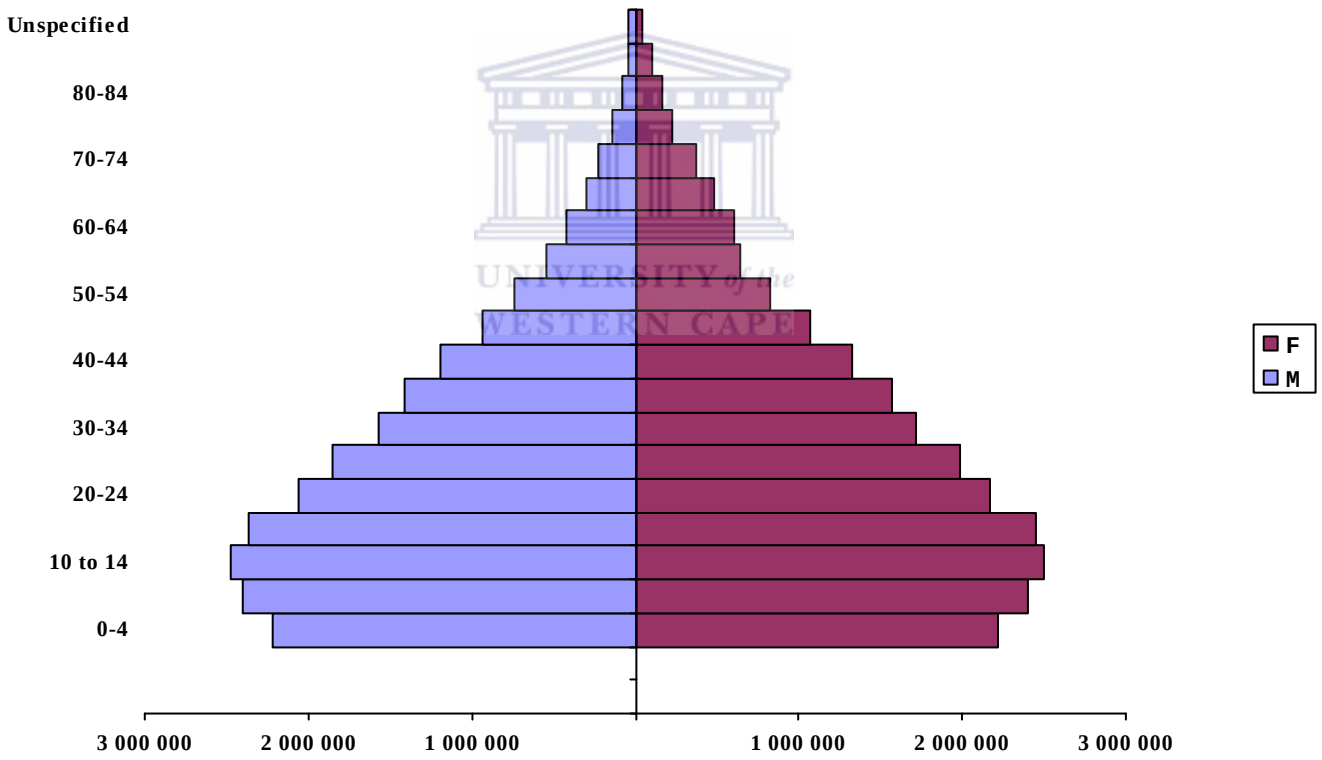

Figure 3. Age distribution of males and females in total population 2000.

Figure 3 shows the distribution of the total population in the year 2000. The females were more than the males and there were fewer number of children in the 0 – 4 age group

compared to the 5 – 9 age groups. This difference could be attributed to increased prenatal deaths or a decline in the fertility rates.

The age distribution for oral cancer cases for this study population was grouped in 5-year categories and it showed a progressive increase in the number of cases with age (figure 4).

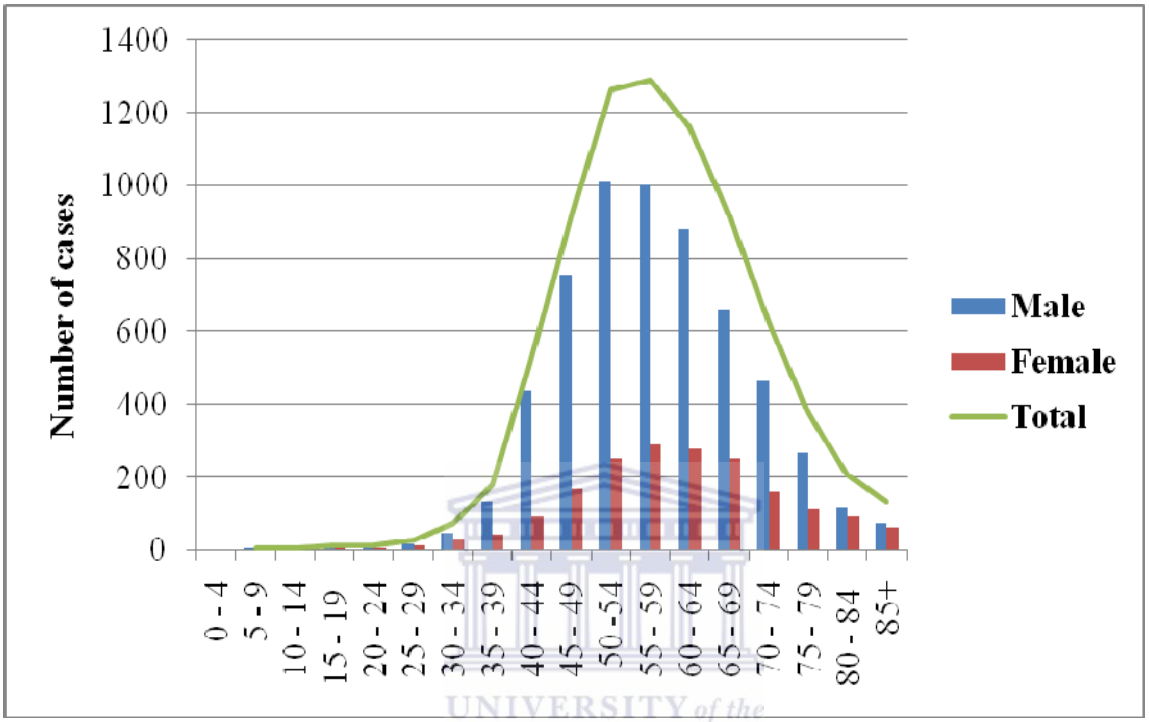

Figure 4. Bar graph depicting oral cancer distribution by 5-year age groups for males and females 1996 – 2002.

From the 55 – 59 age groups onward, the number of oral cancer cases showed a declining trend which corresponds to the population pyramid.

The African and Asian males showed a peak in the 50 – 54 age groups while the coloured and white males experienced their peak in the 55 – 59 age groups as is apparent in figure 5.

The African females showed a peak in the 55 – 59 age group; coloured and whites in 60 – 64 age group and the Asians in the 65 – 69 age group as in figure 6.

Males in the African, coloured and white population groups had their peak occurrence five years earlier than the female counterparts while the Asian males had their peak incidence 10 years earlier than the females.

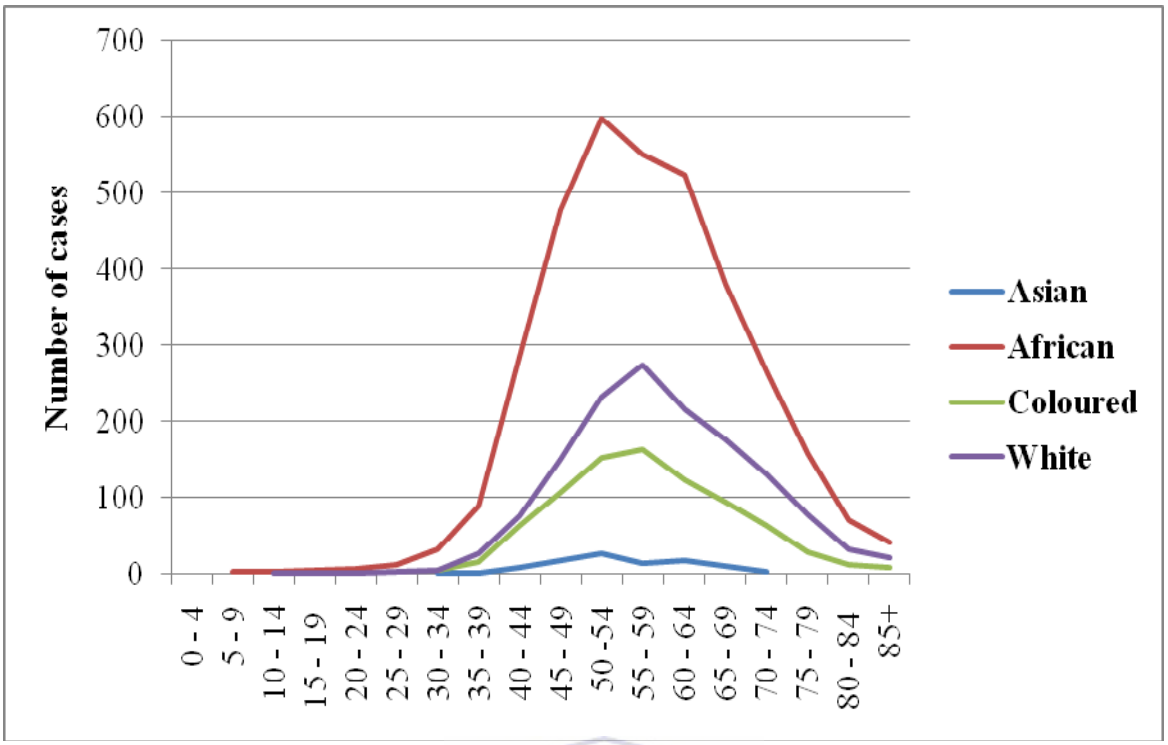

Figure 5 Distribution of oral cancer by 5-year age groups for each population group (males) 1996 – 2002.

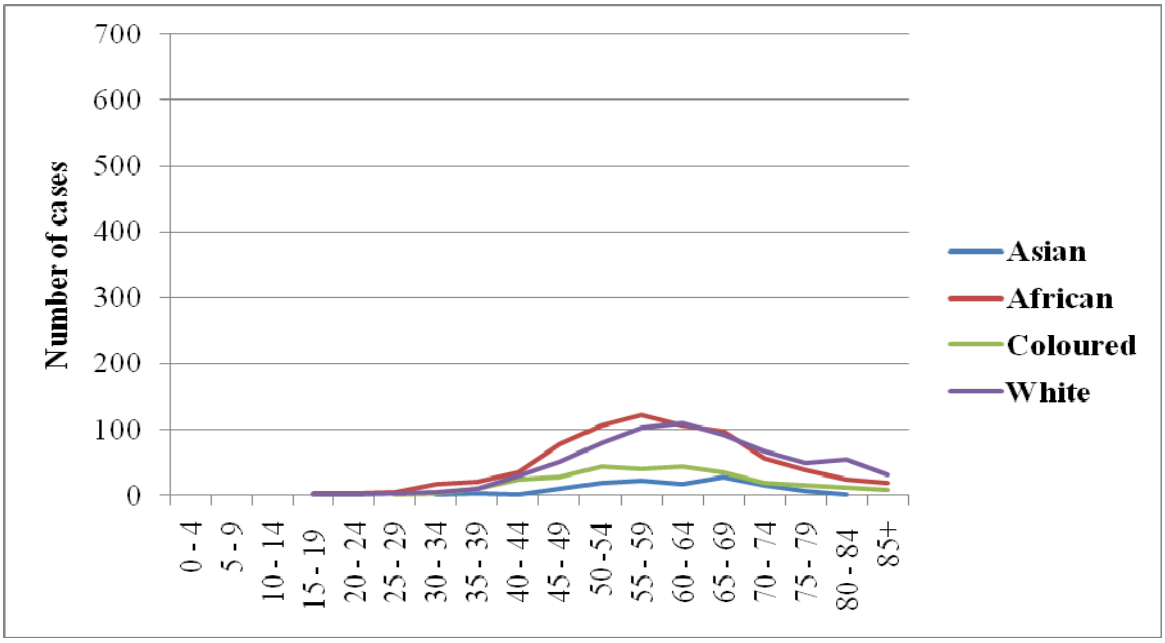

Figure 6. Distribution of oral cancer by 5-year age groups for each population group (females) 1996 – 2002.

In the 0 – 39 age group, the African males had 149 cases of which 121 were in 30 – 39 age groups. The other 3 population groups had a total of 69 cases in 0 – 39 groups (figure 7).

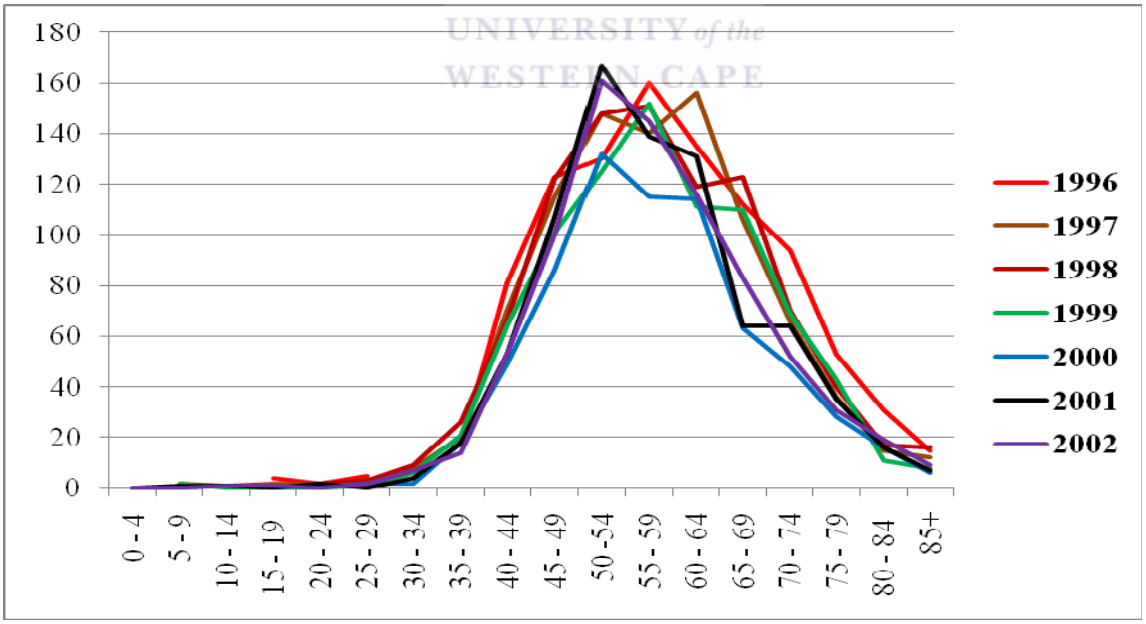

Figure 7. Line graph for trends of oral cancer by 5 – year age groups for all males.

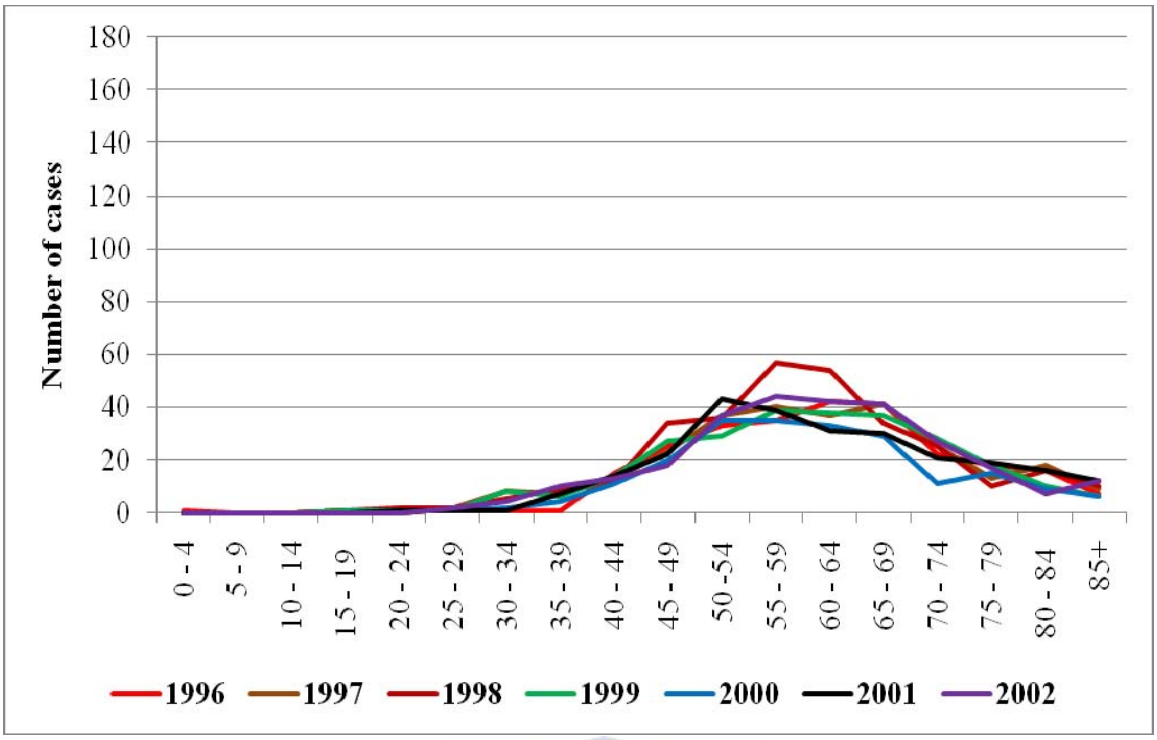

Figure 8. Line graph for trends of oral cancer by 5 – year age groups for all females.

The total number of cases in the 0 – 39 years age group for the females was 75, of which 52% were African females. During the study periods and among the different population groups, there was no increase in the number of new cases in the younger population (<45 years).

The total number of cases in both gender groups was lower in 2000 compared to the other years. There was no indication of a decrease in the total population shown in the population pyramid in figure 3. The population distribution was compared to that of 1999 and 2001 (appendix VIII and IX). The trends of oral cancer for males and females in the African and white population groups is shown in appendix 9 and 10 respectively. The white males had a constant trend while the other three groups showed a rising trend. There was no shift towards the younger age groups.

5.4 Site distribution

The distribution of all reported squamous cell carcinoma cases at different sites over the study period is shown in figure 9.

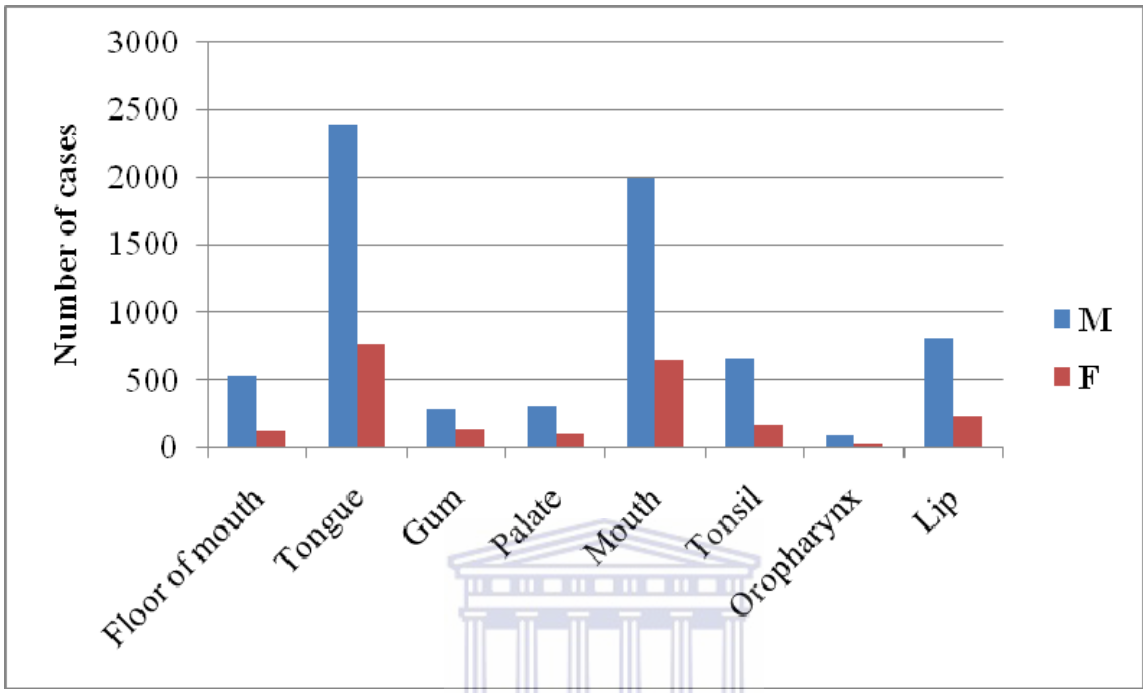

Figure 9. Bar graph showing the distribution of oral squamous cell carcinoma by site and gender for all population groups.

The tongue had the highest number of reported cases (33.9%), followed by the mouth (28.8%) and the oropharynx had the lowest number (1.2%). Oropharyngial and tonsilar squamous cell carcinomas in both males and females showed a rise in numbers from the age of 45 years (figures 10 and 11). A similar trend was recorded for oral cancer. There was no shift of the cancer cases in these two sites towards the younger age groups (figures 10 and 11). Intraoral cancer in this study referred to oral cancer as indicated earlier excluding oropharynx and tonsil cases.

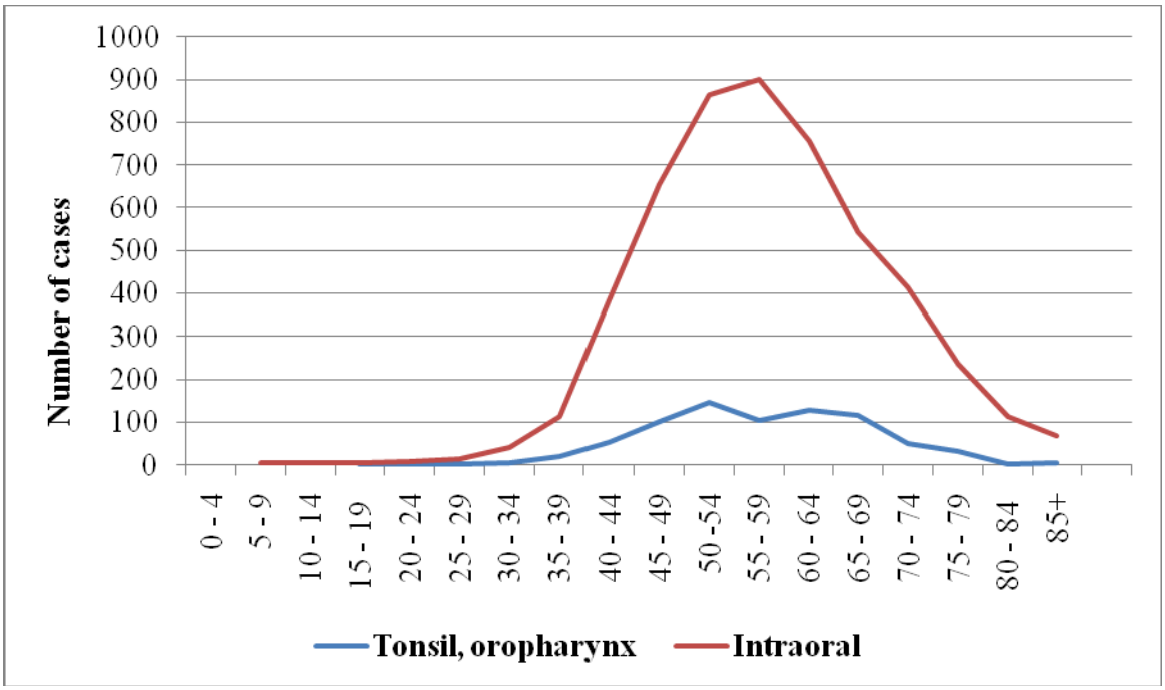

Figure 10. Distribution of oropharyngeal and tonsilar cancer combined, and intraoral cancer for all males.

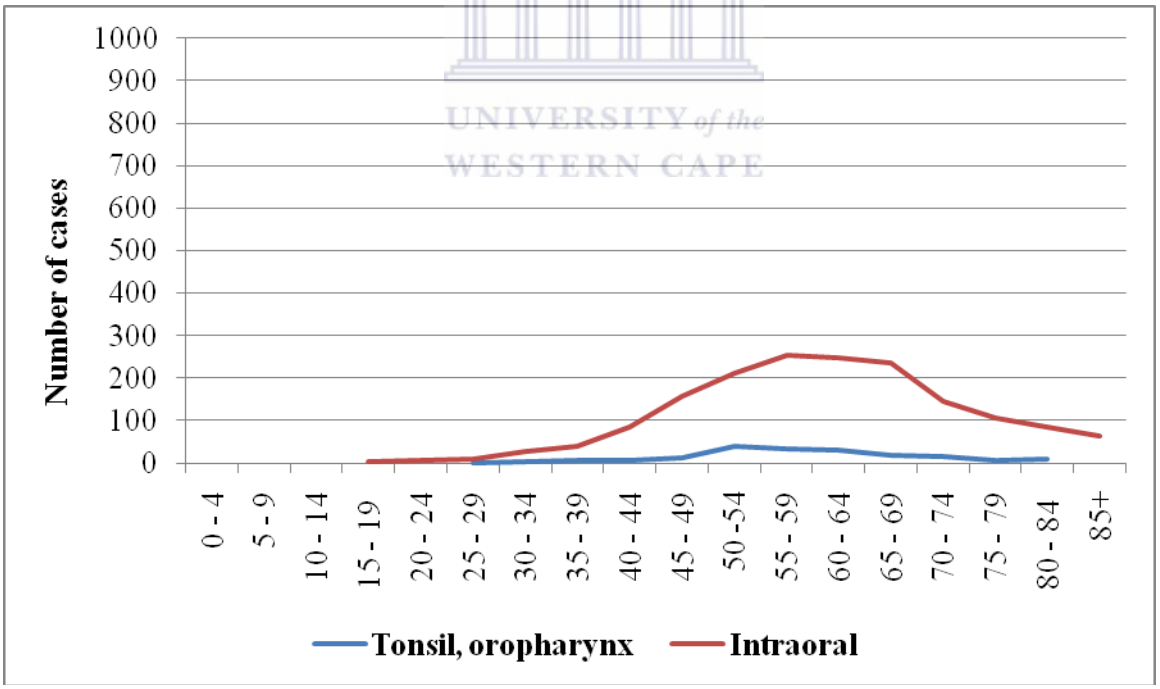

Figure 11. Distribution of oropharyngeal and tonsilar cancer combined, and intraoral cancer for all females.

Lip cancer

Lip cancer cases were recorded in much younger age groups than oral cancer. It showed a slight rise with increasing age among the males. Among the females, the majority of the cases occurred between 60 years and 80 years of age (figure 12). Females represented 22.4% of the total 1038 cases.

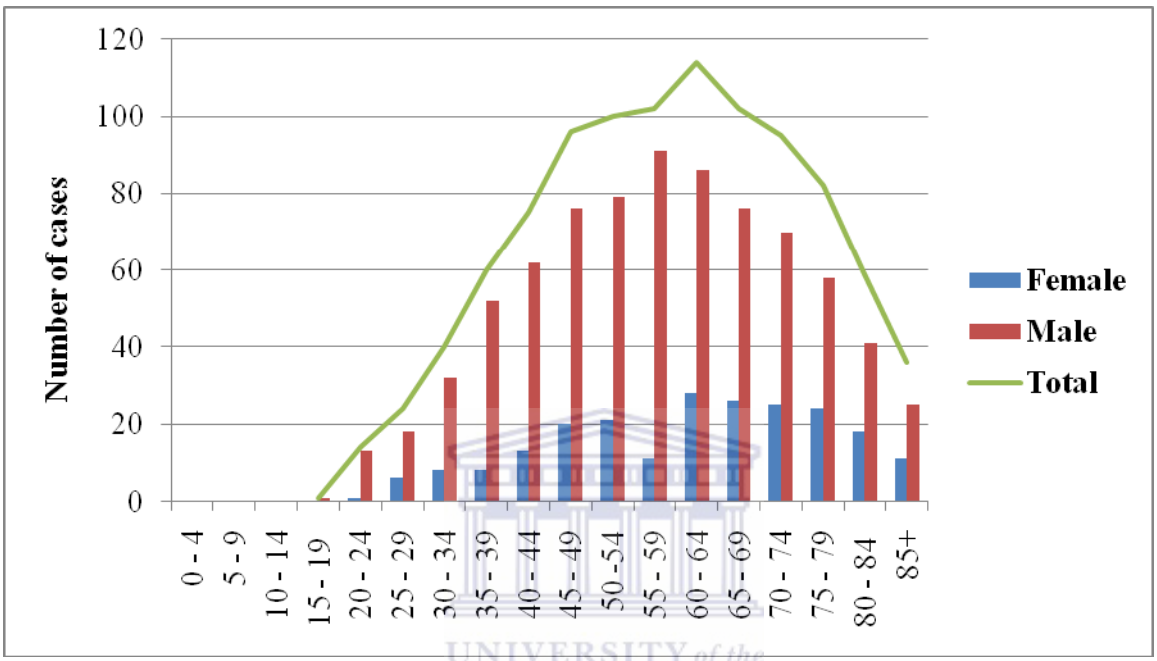

Figure 12. Distribution of lip cancer by 5-year age groups for males and females 1996 – 2002.

There was a marked difference in the number of lip cancer cases among males. The majority of cases occured in the white population – 595 of 722 cases(82.4%). A decline was noted as illustrated in figure 13. The white females also had the highest number of lip cancer cases and showed a similar decline. This is in contrast to oral cancer that was more evident in the African population. Lip cancer in the Asian population remained unchanged (figure 14).

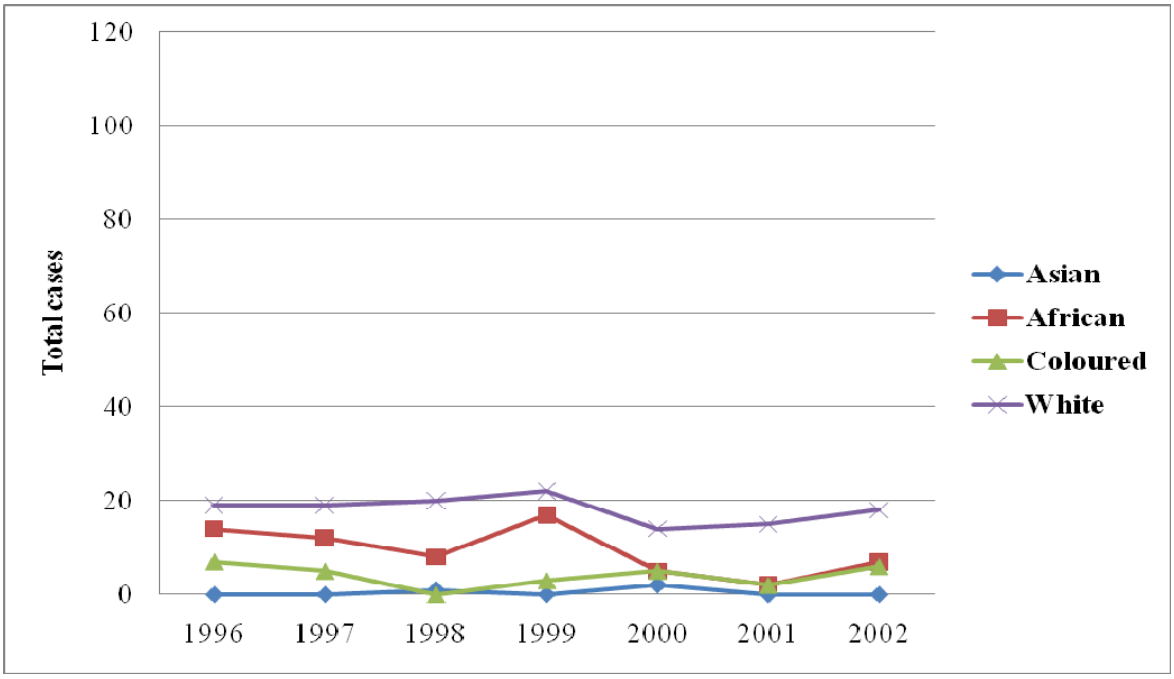

Figure 13. Line graph for trends of lip cancer in all males.

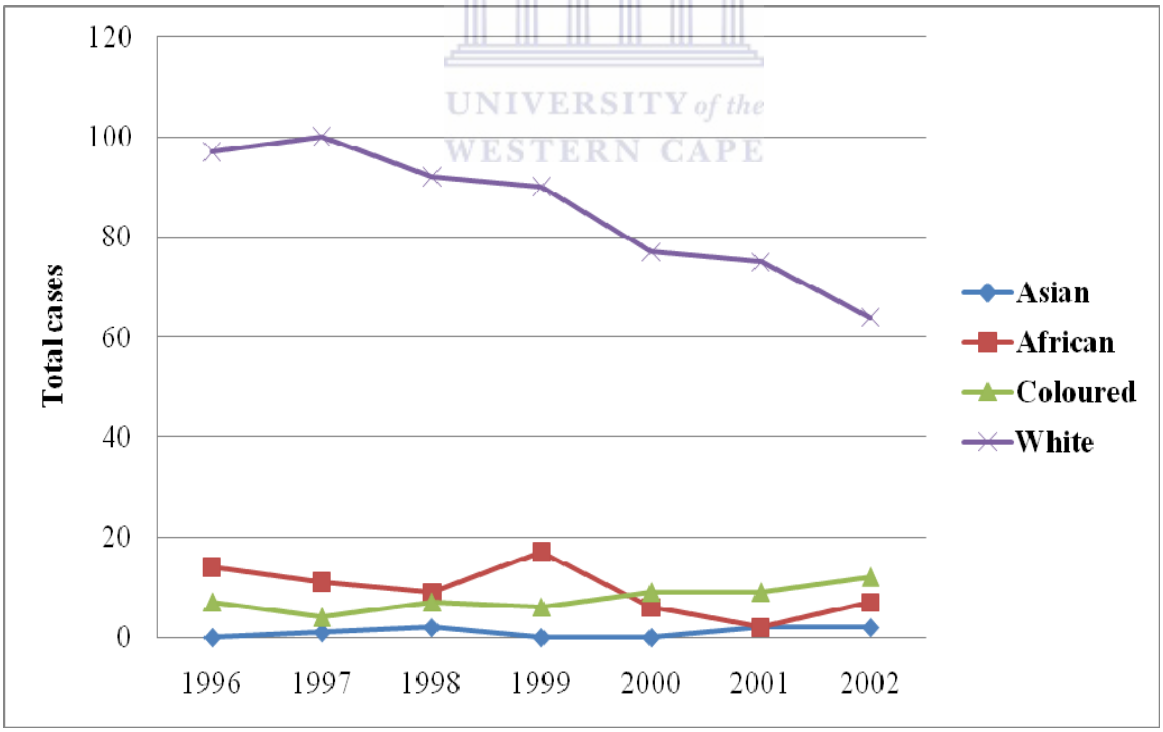

Figure 14. Line graph for trends of lip cancer in all females.

5.5 Incidence rates

Age specific morbidity rate per 100 000 per year for males was highest in the coloured population (figure 15). The range for all males was 0.1 – 1.7 per 100 000 per year. The peak for the age specific morbidity rate was 50 – 54 years for Africans; Asians 60 – 64 years; coloured 60 – 64 years; white 55 – 59 years. The graphs for age specific morbidity rates for males in the different population groups are in appendix XII.

The age specific morbidity rate for females was highest in the Asian population (figure 16). The range was 0.1 – 1.0 per 100 000 per year. The peak was in the 50 – 54 years age group for Africans; Asians 65 – 69 years; coloured 50 – 54 years and 70 – 74 years; whites 60 – 64 years. The graphs for age specific morbidity rates for females in the different population groups are in appendix XIII.

The African males and females had the peak age specific morbidity rate earlier than the other population groups.

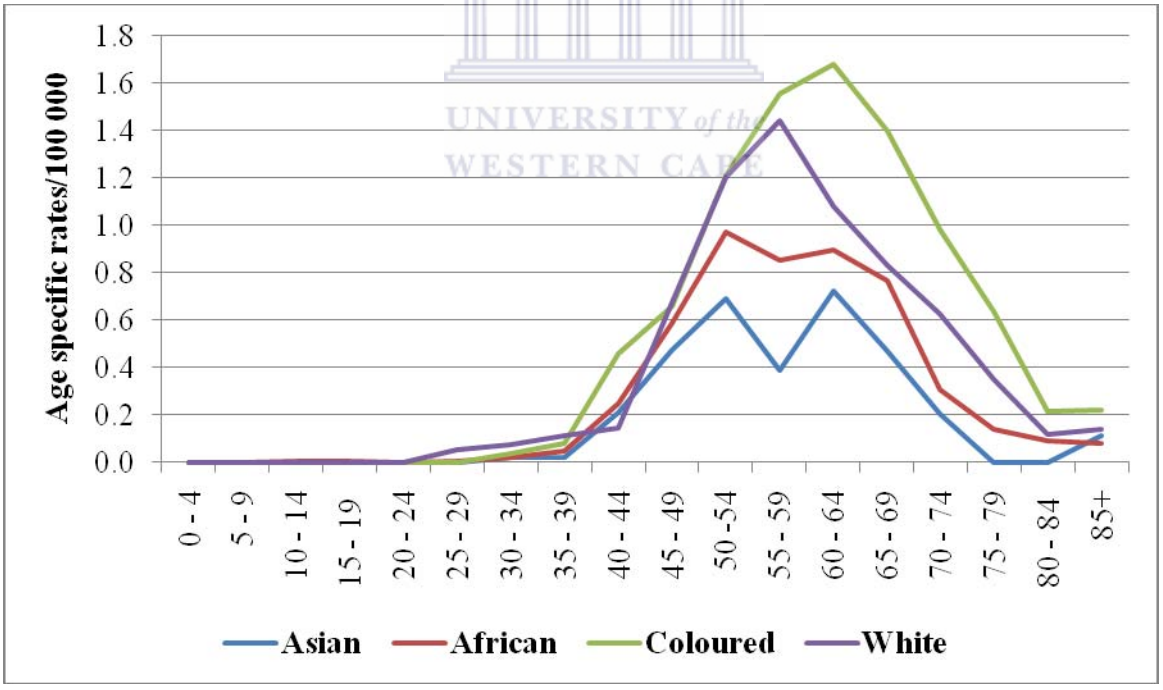

Figure 15. Age specific morbidity rates per 100 000 per year for oral cancer in males.

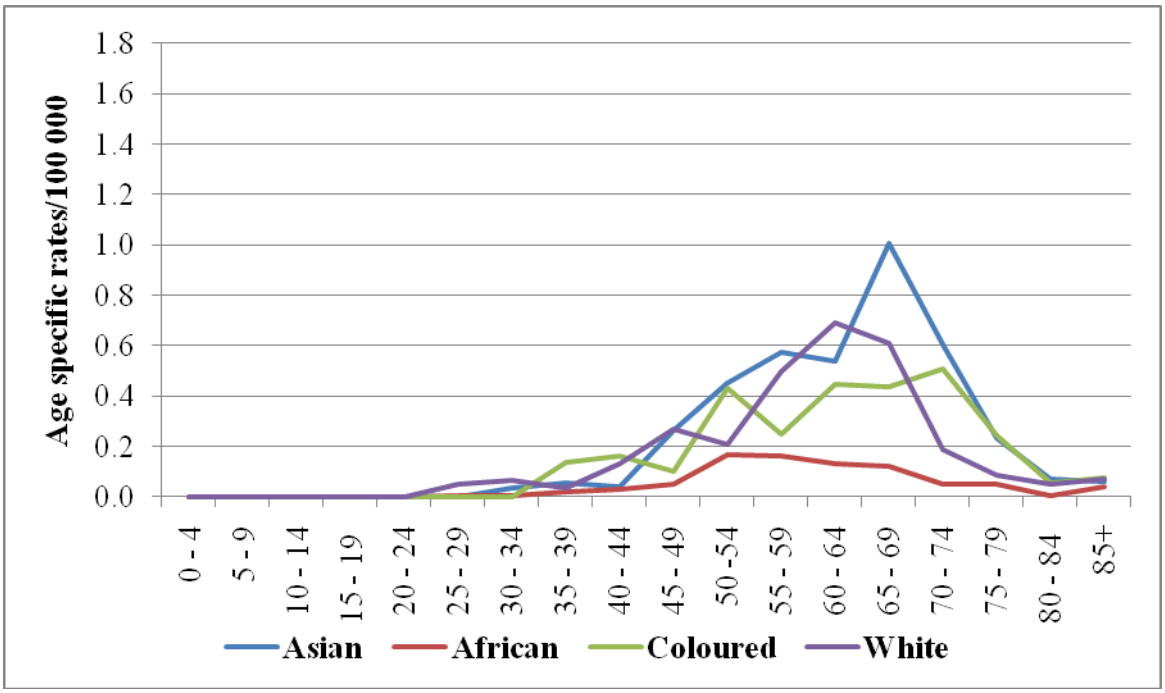

Figure 16. Age specific morbidity rates per 100 000 per year for oral cancer in females.

Age adjusted incidence rates (males)

Figure 17 show the age adjusted incidence rates for the males for oral cancer from 1996 – 2002. The range of the results was 1.87 to 13.40 per 100 000 per year. The lowest age adjusted incidence rate was reported in the Asians while the highest was in coloured population groups. The rates for the Africans showed a gradual decline from 1996 to 2002. The age adjusted incidence rate over the study period for all males was 6.19 per 100 000 per year. The rates were decreasing over the years but the for coloured group it remained constant.

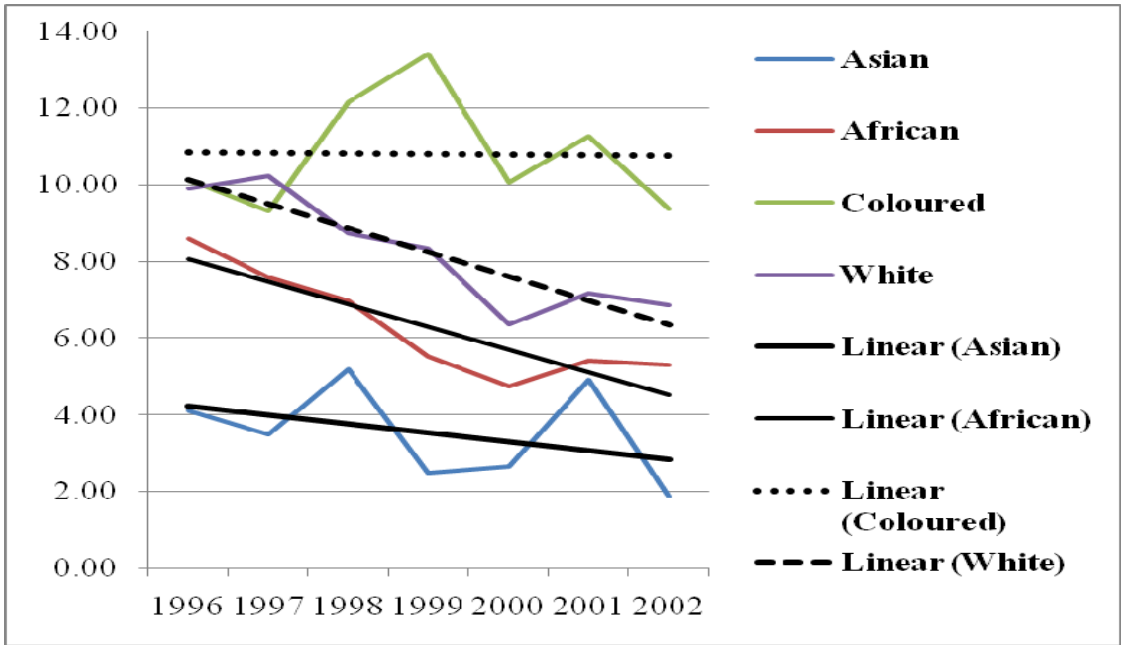

Figure 17. Line graph showing age adjusted incidence rate per 100 000/year for oral cancer in males.

Age adjusted incidence rates (females)

The range for age adjusted incidence rate among the females was 0.69 to 6.97 per 100 000 per year. This was much lower compared with the rates for the males. The Asian women generally had higher age adjusted incidence rate while the lowest rates were among African women (figure 18). The age adjusted incidence rate over the study period for all females was 1.60 per 100 000 per year. The rates demonstrated a declining trend except for the coloured group which had a slight rise.

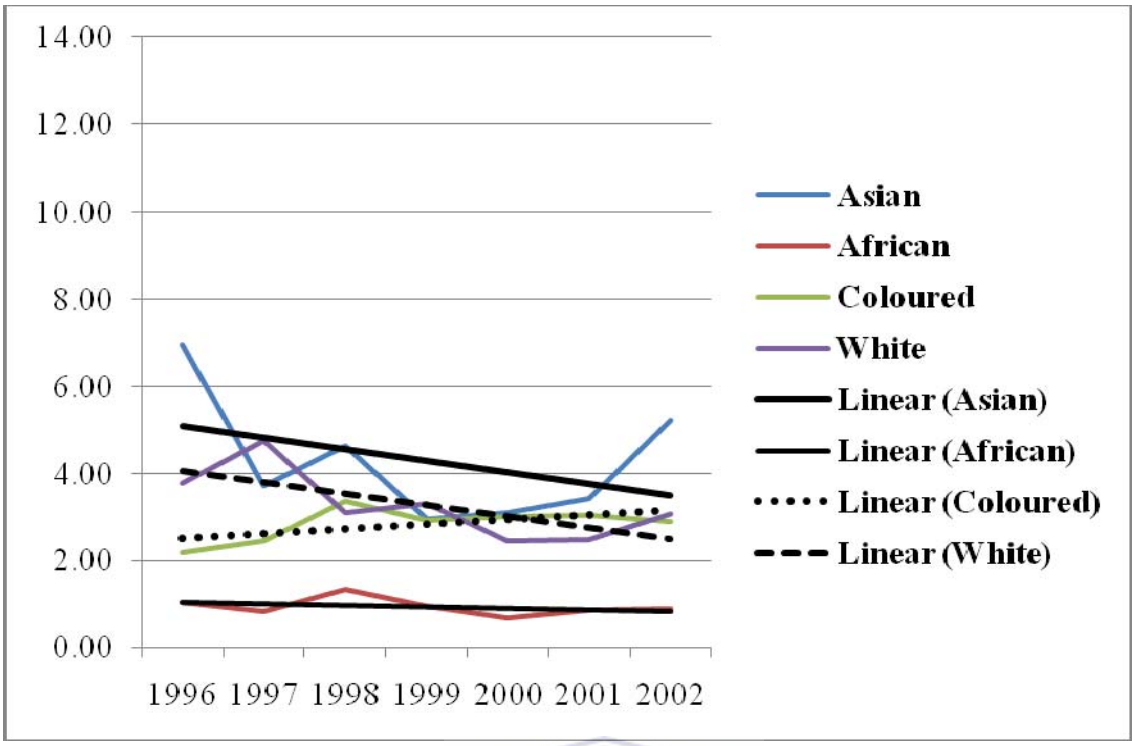

Figure 18. Line graph showing age adjusted incidence rate per 100 000 per year for oral cancer in females.

The cumulative lifetime risk of developing oral cancer varied markedly between the genders. The cumulative lifetime risk for coloured males was 1:49 while the Asian females had 1:120, the highest for each gender.

Lip cancer

The age standardized incidence rate for the lip was calculated separately because of the likelihood of overlap of skin cancers. The white males had a consistently high age standardized incidence rate compared with the other population groups over the 7 years and the Asian males reported the lowest values. The range of the age standardized incidence rate was 0.20 – 3.92 per 100 000/year (figure 19).

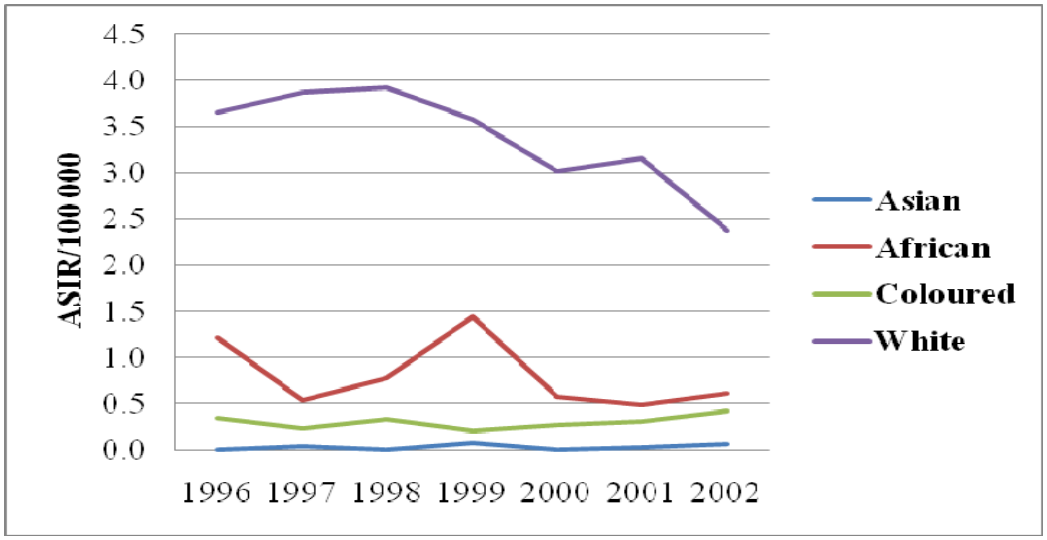

Figure 19. Line graph for age standardized incidence rate for lip cancer in males.

Among the women, age standardized incidence rate for lip cancer were high in the white population followed by the African women (table 6 and figure 20). The peak among Africans was in 1999. The Asian women had very low age standardized incidence rates, which was in contrast to the high rate recorded for intraoral cancer.The distribution of age standardized incidence rates for lip cancer appeared to follow similar pattern in males and females for the population groups, that is in decreasing order white, African, coloured and Asian population groups.

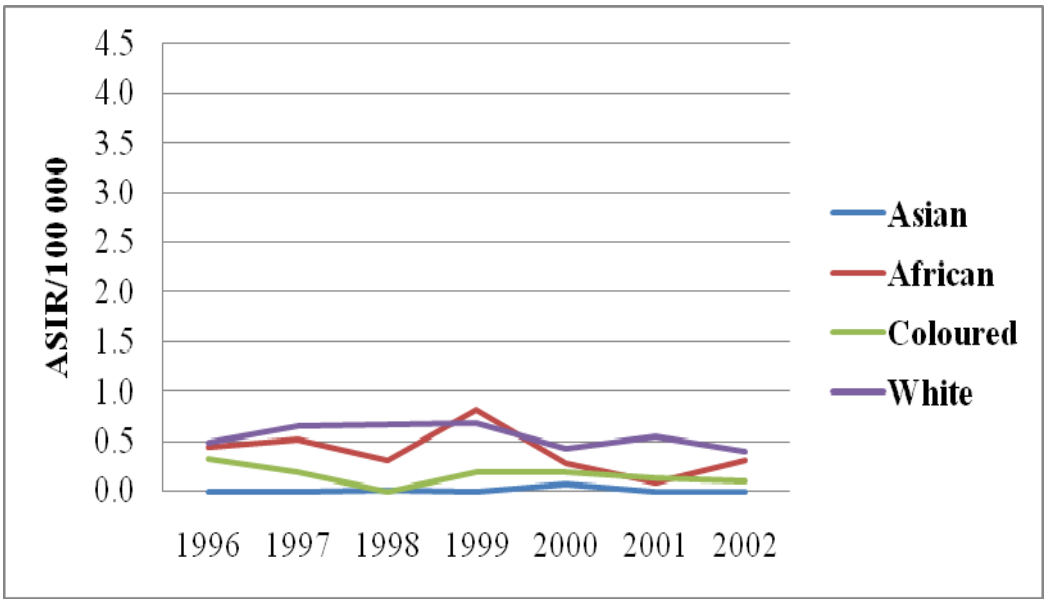

Figure 20. Line graph for age standardized incidence rate for lip cancer in females.

Age standardized incidence rate for oral and lip cancer combined

The age standardized incidence rate per 100 000 per year for each population group over the 7 years period ranged from 0.97 to 11.54. The age standardized incidence rates for males vs females was: Asians 3.60 vs 4.10; Africans 6.14 vs 0.97; coloured 11.54 vs 3.13; white 11.24 vs 3.70. The age standardized incidence rates for all the sites combined for each year indicated high rates among the white and coloured population and lower rates in the African and Asian population (figures 21 to 24). Women had lower rates than the men except for the Asian women. The 95% confidence intervals were wide among the Asians reflecting the few number of cases over the study period.

Estimates of the ASIR for oral and lip cancer combined and 95% confidence intervals.

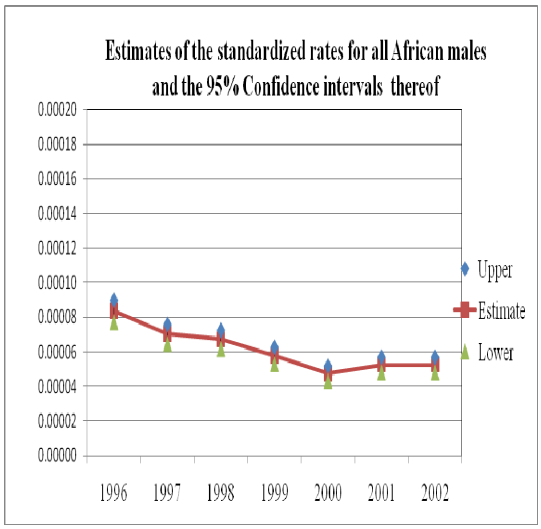

Figure 21(a)

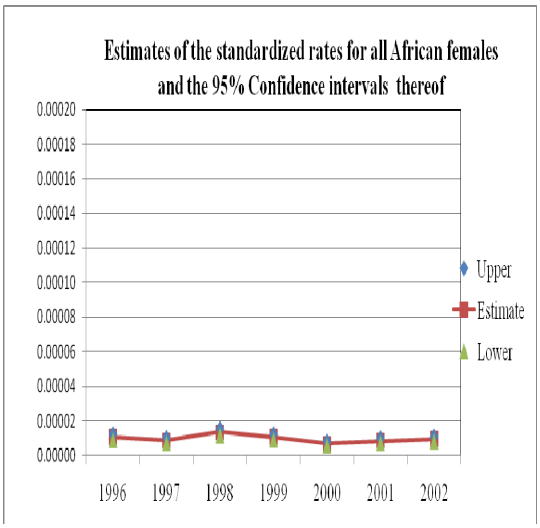

Figure 21(b)

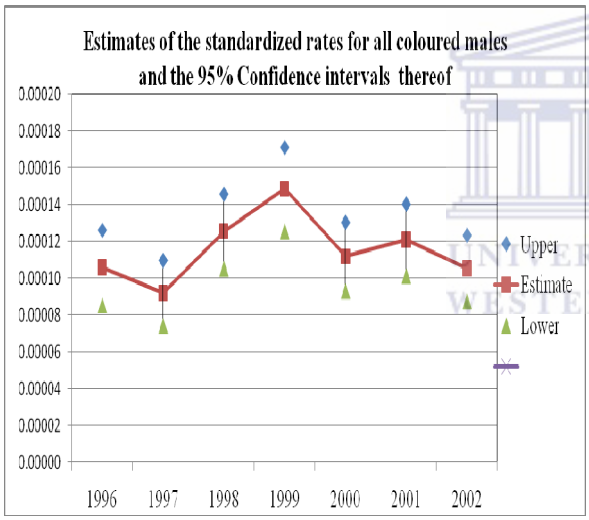

Figure 22(a)

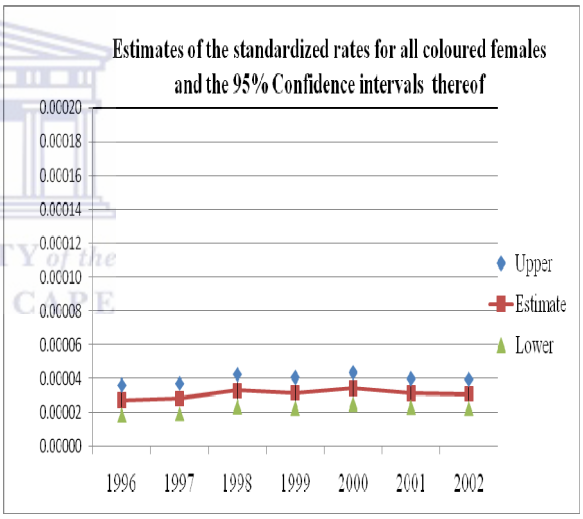

Figure 22(b)

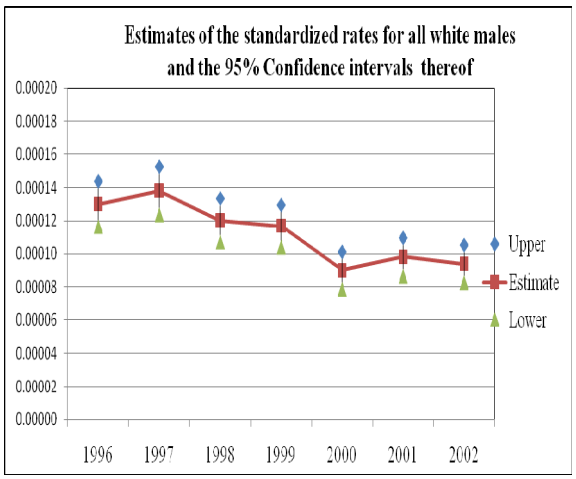

Figure 23(a)

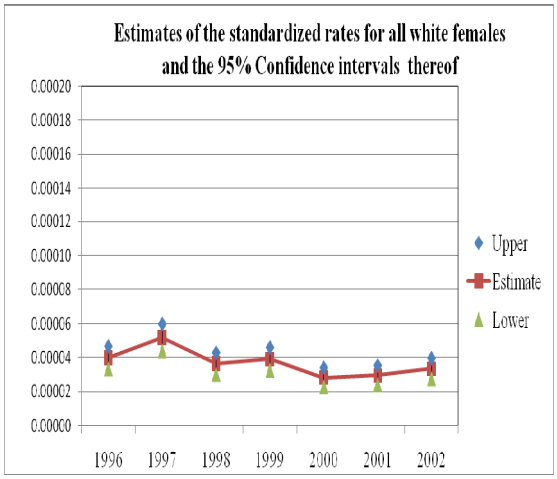

Figure23(b)

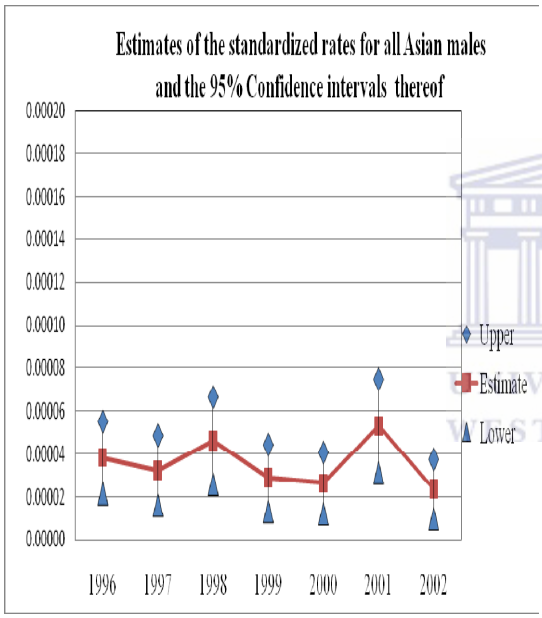

Figure 24(a)

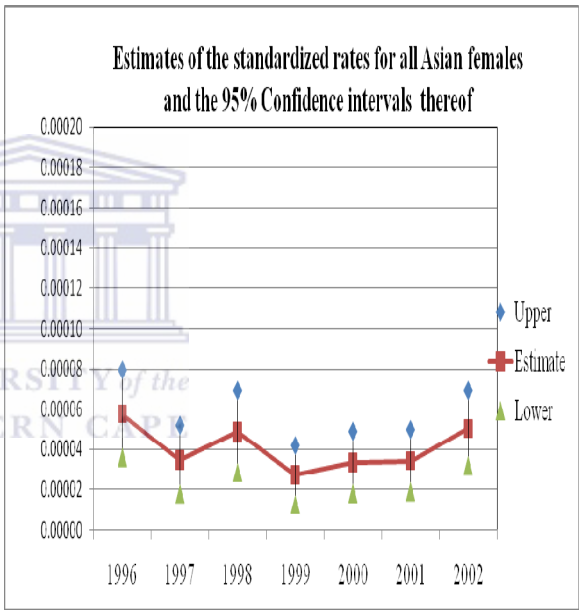

Figure 24(b)

Figures 21 – 24 illustrated the 95% confidence intervals for the age standardized incidence rates for oral cancer in males and females in the four population groups.

CHAPTER 6

DISCUSSION

The total number of oral squamous cell carcinoma cases as recorded by the National Cancer Registry over the 7 year period was 9702. This was 8.4% higher than the 8950 reported cases in 1988 – 1995 study on epidemiology of oral cancer in South Africa. Females represented 23.69% and males 76.31% in this study while in 1988 – 1995 there was 26.34% and 73.66% respectively (Hille and Shear, 2001). The male to female ratio was 1:3 for this study and for 1988 – 1995 periods it was 1:2.8. The gender ratio conformed to the worldwide trends being within the ranges reported in other studies (Marur and Forastiere, 2008; Neville *et al*., 2009; Iamaroon *et al*., 2004).

6.1 Oral cancer

The age specific morbidity rates had a range of 0.1 – 1.7 per 100000 per year in males. The rates among the men were highest in the coloured group with almost no overlap with other population groups. The Asians had a lower rate than the Africans. Among the females, the range was 0.1 – 1.0 per 100000 per year. Asian women had the highest rates with some overlap with the whites, and the African women had a consistently low rate. This was a similar trend to the previous South African studies (Hille and Shear, 2001; Hille *et al.*, 1996). The early peak for African males (50 – 54 years) and the later peak in coloured and Asians (60 – 64 years) could be attributed to early exposure to causative factors or varying habits. The coloured population had more cancer cases from 65+ years than the other population groups. The African females had the peak rate at 50 – 55 years while Asians had the peak at 65 – 69 years. This probably was a result of the duration it takes for the effects betel nut chewing to cause dysplastic changes in the oral cavity. Betel nut chewing is a habit prevalent among Asian females.

The age adjusted incidence rates in this study for males had a range from 1.87 (Asian) to 13.40 (coloured) per 100 000 per year, and 6.19 for all males. This showed a decrease of oral cancer among the Asian male population and a rise among coloured males. In the 1993 – 1995 period, the age adjusted rates were 4.49 (Asian) and 8.85 (coloured) per 100 000 per year, and 8.15 for all males (Hille and Shear, 2001). Among the females, age adjusted incidence rate in 1996 – 2002 for the African and Asian was 0.93 and 4.19 per 100 000 per

year respectively, and 1.60 for all females. There was a decrease compared to 1993 – 1995 rates of 1.10 and 8.88 for the Africans and Asians, and 2.01 for all females (Hille and Shear, 2001). The decline in the age adjusted rates in Asian, African and white males, and Asian and white females was probably an indication of reduced involvement in habits associated with aetiology of oral cancer. The slight rise in coloured females could reflect an increase in smoking or other causative habits. The trend in African females did not change; they had a low number of cases and lowest rates similar to those reported in previous South African studies. Lack of reporting for treatment or lack of involvement in causative habits might explain this trend.

Robinson and Macfarlane (2003) reported an increase in the age standardized incidence rate (ASIR) from 9.5 to 11.5 in males and 3.8 to 4.8 per 100 000 per year in females in Scotland in 1989-1996; this was slightly lower than South African coloured males (13.40) but higher than the rates recorded for South African women (except Asians) in this study. The ASIR for males and females in Uganda and Algeria 1988 – 1992 was 1.2 and 1.9, and 1.1 and 0.3 per 100 000 per year respectively (Franceschi *et al*., 2000). In Zimbabwe, the ASIR for intraoral cancer for the period of 1988-2000 for male and female were 1.09 and 0.51 per 100 000 per year respectively (Marimo and Hille, 2006). The rates in the three African countries are much lower than the South African rates for men and women. A possible reason for this could be under reporting especially when using hospital data.

In 2002, the world age standardized incidence rate for oral cavity cancer for males and females respectively was 6.3 and 3.2 per 100 000 per year (Parkin *et al*., 2002). The rate for males was lower than that of coloured and white South African males (10.82 and 8.19) respectively but close to that of African males (6.19) for 1996 – 2002. The world rate for females was similar to that of South African white females but lower than for South African Asian females (4.19) and 2 times the overall rate for all South African females (1.60). According to the SEER data (Brown *et al.,* 2010) the black males in the United States had the highest age standardized incidence rate (8.6) while in the South African population the blacks had a rate of 6.19, with the coloured and white males having 10.82 and 8.19 respectively. These rates displayed the geographic and cultural differences between the South African and United States populations. The age standardized incidence rates per 100 000 per year for various world populations were compared to those for South African population (appendix XIV).

Racial differences have been cited in the incidence of head and neck cancer with the African American being affected more than the white population for both males and females (Marur and Forastiere, 2008; Franceschi *et al*., 2000). These differences were also reflected in our study. African males accounted for 42.26% and white males 22.69% of all cases. Africans represented 9.42% and the white females 9.18% of all cases. In the 1988 – 1995 study, African males represented 47.42% and white males 16.73% of all oral squamous cell carcinoma cases (Hille and Shear, 2001). These differences could be attributed to social and cultural practices or the fact that the African males were the majority in the total population.

Compared with 1993-1995 period, the cumulative lifetime risk of developing oral cancer increased for all groups except the Asians, the decrease however was not remarkable. The coloured females showed a marked increase; 1:435 (1993-1995) to 1:162 (1996-2002). The rise was likely as a result of increased cigarette smoking in this group. Cumulative lifetime risk for coloured males was 1:49, remaining and similar to that reported in previous studies. The table comparing our results with previous South African studies is in appendix XV.

6.2 Age

Age distribution of all cases showed a progressive increase in number of new cases with increasing age, with a sharp rise from 40-44 years which was followed by a gradual drop from the 65-69 age group. An increase in cancer incidence in the 40-50 age groups and a decline from the 60-70 age groups has been reported in several studies (Müller *et al*., 2008; Alvarenga *et al*., 2008). Other studies have reported a rise through to the age of 75 years (Carvalho *et al.,* 2005).

There was slightly lower percentage of young people (less than 45 years) with oral cancer in this study compared with a previous South African study 1988 - 1991. In 1996 – 2002, 11.19% males and 10.04% females were less than 45 years of age while in 1988 – 1991, 15.6% were males and 14.1% were females (figures calculated from the 1988-1991 study) (Hille *et al.,* 1996). This is in contrast with a study carried out in Thailand which demonstrated an increase in oral cancer among young people in 1991 – 2000, from 4% to 12% (Iamaroon *et al*., 2004). In the study comparing the cases of oral cancer in young Americans between 1973 – 1984 and 1985 – 1997, the results showed a 62% increase in young people, with tongue cancer being the most frequent (Schantz and Yu, 2002). The

constantly low number of oral cancer cases among younger people and in the general population could imply that human immunodeficiency virus (HIV) infection has had no influence on the occurrence of oral squamous cell carcinoma, considering the high rates of HIV infection reported in South Africa.

When oropharynx and tonsil cancer cases for males and females were tabulated (figures 10 and 11), there was no evidence of increased cancer cases compared to previous South African studies. It showed the same age distribution as intraoral cancer. These results are in contrast to a study in Scotland, which showed an increase in oral and pharyngeal cancers by 31% in males and 16% in females between 1989 – 1996 (Robinson and Macfarlane, 2002). Varying proportions of oropharyngeal and tonsillar squamous cell carcinoma cases have been associated to the human papillomavirus (Herrero *et al*., 2003; Gillison, 2004; McKaig *et al*., 1998). The constantly low incidence of oropharyngeal and tonsillar squamous cell carcinomas and the high incidence in the older age group in the South African population could imply that human papillomavirus does not influence the occurrence of these tumour. However, additional and more sophisticated studies would be necessary to confirm this inference.

6.3 Anatomical sites

The most common site of squamous cell carcinoma was the tongue (33.88%) followed by the mouth (28.75%). The lip represented 11.05%. These results were similar to a study performed in Kenya that showed the tongue to be the predominant site, followed by the mandible, maxilla and lower lip in decreasing frequency (Onyango *et al*., 2004). Other African studies also concurred with these results (Llewellyn *et al*., 2003; Müller *et al*., 2008; Davies and Welch, 2006; Marimo and Hille, 2006; Hirota *et al*., 2008), so did reports among European and United States populations (Warnakukasiriya, S., 2009b).

A study on incidence and trends of head and neck cancer in America found an increase in tongue cancer among those less than 40 years old (Schantz and Yu, 2002). This on the other hand is in contrast to our findings where cases of tongue cancer increased from the age of 40 years and a decline in the 70’s, having a similar trend to the other intraoral sites.

Although our study was not investigating the etiologic factors of squamous cell carcinoma, none of these other studies explained their findings on the predominant sites.

6.4 Lip cancer

The lip lesions are reported separately in some studies owing to the different pathogenesis (Hille and Shear, 2001; Carvalho *et al.*, 2005). In this study, the white population had the highest proportion of lip cancer, with the males and females representing 82.41% and 56.95%, and incidence rates of 3.92 vs 0.68 respectively. In comparison to previous studies (appendix III and IV, there was a remarkable decrease in the age standardized incidence rates among the females compared to the men (Hille *et al.*, 1996; Hille and Shear, 2001). High incidence rates in white population compared with non-white population was also reported in Canada and Australia (Warnakulasiriya, S., 2009b).

An important etiologic factor for lip cancer is exposure to ultra – violet irradiation from the sun.

6.5 Oral and lip cancer combined

The age standardized incidence rate for all ages and sites 1996 – 2002 for males vs females was Asian 3.60 vs 4.10; African 6.14 vs 0.97; coloured 11.54 vs 3.13; white 11.24 vs 3.70. The worldwide age standardized incidence rate per 100 000 for several regions in 2000 in males and females was reported (Ferlay *et al*., 2000). Namibia had 34.17 vs 11.71; United States of America 9.32 vs 4.35; India 22.4 vs 9.31 and Taiwan 26.98 vs 2.85. The worldwide ASIR for the oral cavity cancers was reported as 6.3 and 3.2/100000/year for males and females in 2002 (Parkin *et al*., 2005).

These worldwide results showed varying rates in men and women compared to those reported for this study. This likely reflects variations in geographic distribution and habits related to aetiology of oral cancer.

The 95% confidence interval was used to compare the different population groups. From these figures, it can be inferred that there were substantial differences in the age standardized incidence rates between the males and females in all groups except the Asians. The differences could be significant, but this could not be confidently stated because no statistical tests were done. Coloured males had the highest incidence rates like in previous South African studies (Hille *et al.*, 1996).

CHAPTER 7

LIMITATIONS OF THE STUDY

This study utilized data that had been compiled by the National Cancer registry. The registry extracts data from the pathology reports sent by private and public laboratories. Some laboratories may send incomplete data which may lead to incorrect reporting.

The compiled report from the National Cancer Registry fell far short of the intended study period. The initial aim was to determine the pattern and incidence of oral cancer in South Africa 1996 - 2005, but the registry provided data for seven years, 1996 – 2002. Although the data provided was used for assessment of the trends, a longer period would have given a broader view of any changes occurring in the incidence of oral squamous cell carcinoma.

CHAPTER 8

CONCLUSIONS

The male to female ratio was 3:1, similar to prior South African studies. The most common site for oral cancer was the tongue followed closely by the mouth.

This study has demonstrated the trends of oral cancer between 1996 and 2002. There was a downward trend in the incidence of oral cancer among the Asian, African and white males but the coloured males had consistently high incidence rate. Among the females, there was a declining trend in the Asians and whites but a rise in the coloured population. The African females had a consistently low incidence rate. The varied trends could be an indication of a change in their involvement in habits that contribute to occurrence of oral cancer or changes in the reporting patterns.

The incidence rate among coloured males was higher than 1993 – 1995 periods. Although the incidence rate in the Asian females in our study was lower incidence than 1993 – 1995 periods, it remained the highest among the females. There was a notable rise in the cumulative lifetime risk among coloured males and females, and a rise in both genders. The risk of developing oral cancer for Asian females was 5 times that of the African counterparts.

The incidence rate for South African Asian males was similar to that of Asian/Pacific Islander males while the female Asians had double the rate of the Asian/Pacific Islander female. The United States male and female blacks higher rates than the South African black population. This was an indication of the worldwide geographic and habits variations in distribution of oral cancer.

There was no evidence of increase in the new cases of tonsillar and oropharynx squamous cell carcinoma over the study period in the South African population or a shift towards the younger people (aged <45). This could imply that human papillomavirus had not influenced occurrence of cancer in these sites in this population.

The absence of an obvious rise in the incidence of oral squamous cell carcinoma cases in the South African population for all ages could imply that the human immunodeficiency

virus infection has not had an impact on the occurrence of oral squamous cell carcinoma or that the practising of contributing habits remained consistent.

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APPENDICES

Appendix I

ICD-10 NOMENCALTURE OF TOPOGRAPHY:

MALIGNANT NEOPLASMS OF LIP, ORAL CAVITY AND PHARYNX (C00-C14)

C00 malignant neoplasm of lip

Excludes: skin of lip

C00.0 External upper lip

Upper lip:

NOS

Lipstick area

Vermilion border

C00.1 External lower lip

Lower lip:

NOS

Lipstick area

Vermilion border

C00.2 External lip, unspecified

Vermilion border NOS

C00.3 Upper lip, inner aspect

Upper lip:

Buccal aspect

Frenulum

Mucosa

Oral aspect

C00.4 Lower lip

Lower lip:

Buccal aspect

Frenulum

Mucosa

Oral aspect

C00.5 Lip, unspecified, inner aspect

Lip, not specified whether upper or lower:

Buccal aspect

Frenulum

Mucosa

Oral aspect

C00.6 Commisure of lip

C00.8 Overlapping lesion of lip

C00.9 Lip, unspecified

C01 Malignant neoplasm of base of tongue

Dorsal surface of base of tongue

Fixed part of tongue NOS

Posterior third of tongue

C02 malignant neoplasm of other and unspecified parts of tongue

C02.0 dorsal surface of tongue

Anterior two-thirds of tongue, dorsal surface

Excludes: dorsal surface of base of tongue

C02.1 border of tongue

Tip of tongue

C02.2 Ventral surface of tongue

Anterior two-thirds of tongue, ventral surface

Frenulum linguae

C02.3 Anterior two-thirds of tongue, part unspecified

Middle third of tongue NOS

Mobile part of tongue NOS

C02.4 Lingual tonsil

Excludes: tonsil NOS

C02.8 Overlapping lesion of tongue

Malignant neoplasm of tongue whose point of origin cannot be classified to any one of the categories C01-C02.4

C02.9 Tongue, unspecified

C03 Malignant neoplasm of gum

I**ncludes**: alveolar (ridge) mucosa, gingival

Excludes: malignant odontogenic neoplasms

C03.0 Upper gum

C03.1 Lower gum

C03.9 Gum, unspecified

C04 Malignant neoplasm of floor of mouth

C04.0 Anterior floor of mouth

Anterior to the premolar-canine junction

C04.1 Lateral floor of mouth

C04.8 Overlapping lesion of floor of mouth

C04.9 Floor of mouth, unspecified

C05 Malignant neoplasm of palate

C05.0 Hard palate

C05.1 Soft palate

Excludes: nasopharyngeal surface of soft palate

C05.2 Uvula

C05.8 Overlapping lesion of palate

C05.9 Palate, unspecified

Roof of mouth

C06 Malignant neoplasm of other and unspecified parts of mouth

C06.0 Cheek mucosa

Buccal mucosa NOS

Internal cheek

C06.1 Vestibule of mouth

Buccal sulcus (upper) (lower)

Labial sulcus (upper) (lower)

C06.2 Retromolar area

C06.8 Overlapping lesion of other and unspecified parts of mouth

C06.9 Mouth, unspecified

Minor salivary gland, unspecified site

Oral cavity NO

Appendix II

Age interval	1	2	3	4	5	6	7	8	Total
01_0 to 4							1		**1**
02_5 to 9		4					2		**6**
03_10 to 14		4					1		**5**
04_15 to 19		7	1			1	3		**12**
05_20 to 24		3	15	3		1	6		**28**
06_25 to 29	1	10	25	4		3	9		**52**
07_30 to 34	4	34	39	5	6	8	29	2	**127**
08_35 to 39	11	75	61	6	9	28	60	1	**251**
09_40 to 44	42	227	76	27	31	56	172	7	**638**
10_45 to 49	89	368	102	49	37	103	315	16	**1079**
11_50 to 54	117	526	102	58	71	171	384	24	**1453**
12_55 to 59	125	533	105	52	73	129	421	17	**1455**
13_60 to 64	92	452	116	49	59	138	413	23	**1342**
14_65 to 69	68	372	104	55	55	94	317	10	**1075**
15_70 to 74	45	238	100	42	20	61	237	7	**750**
16_75 to 79	32	151	84	30	15	33	138	4	**487**
17_80 to 84	13	86	55	21	16	9	75	3	**278**
18_85+	4	51	41	19	7	9	46	2	**179**
(Unknown)	39	146	46	19	17	54	160	3	**484**
Total	**682**	**3287**	**1072**	**439**	**416**	**898**	**2789**	**119**	**9702**

Frequency of oral and lip cancer by 5-year age groups and anatomic site

1 – Floor of mouth

2 – Tongue

3 – Lip

4 – Gum

5 – Palate

6 – Tonsil

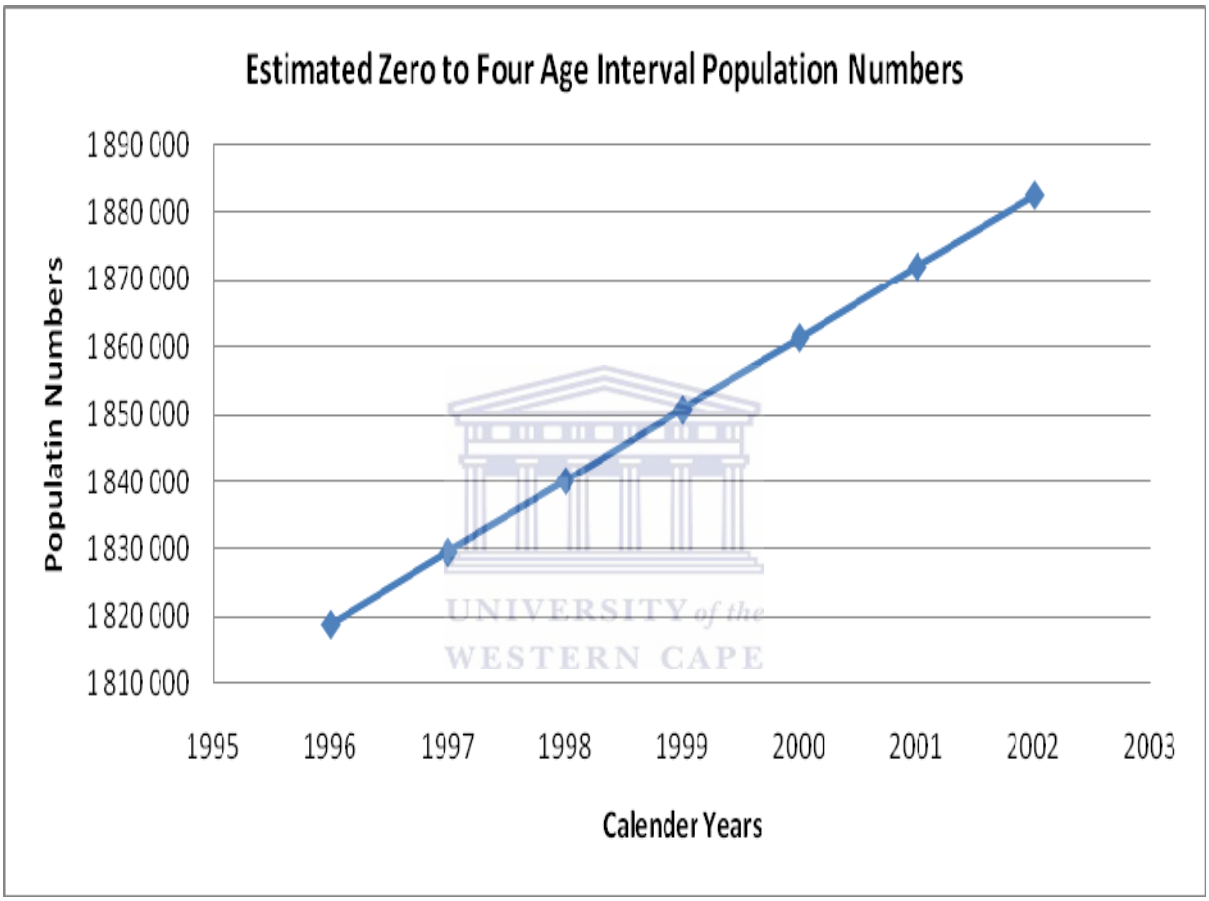
7 – Mouth

8 - Oropharynx

Appendix III

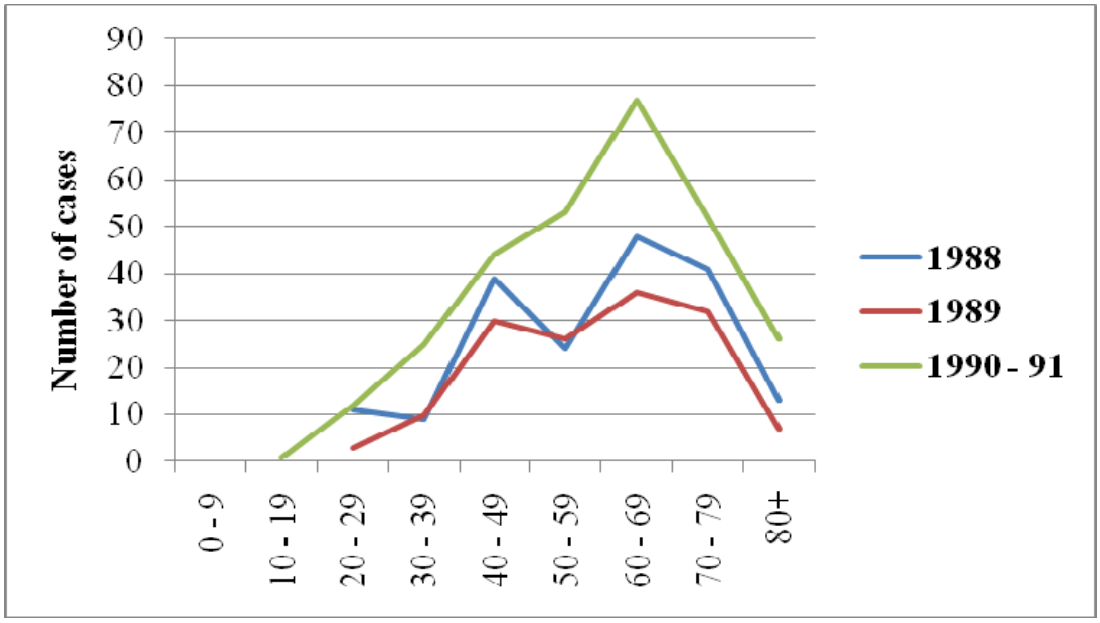
Black Males Linear Interpolation

1996	**1997**	**1998**	**1999**	**2000**	**2001**	**2002**
1818977	1829571	1840166	1850760	1861355	1871949	1882543



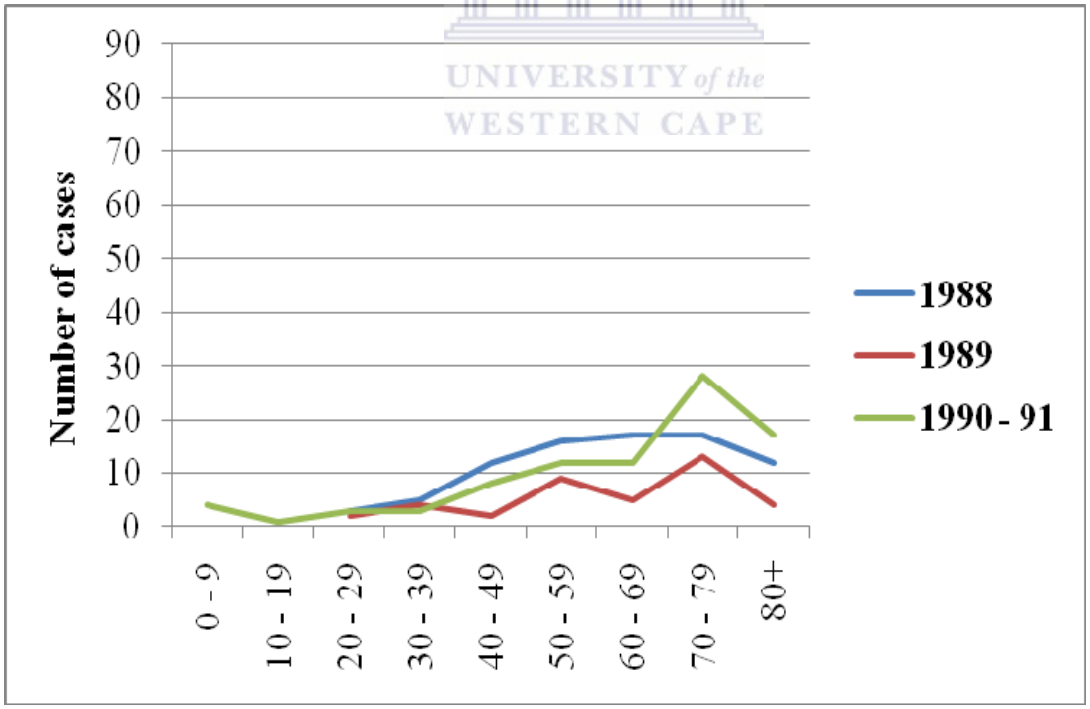
Population linear interpolation

Appendix IV



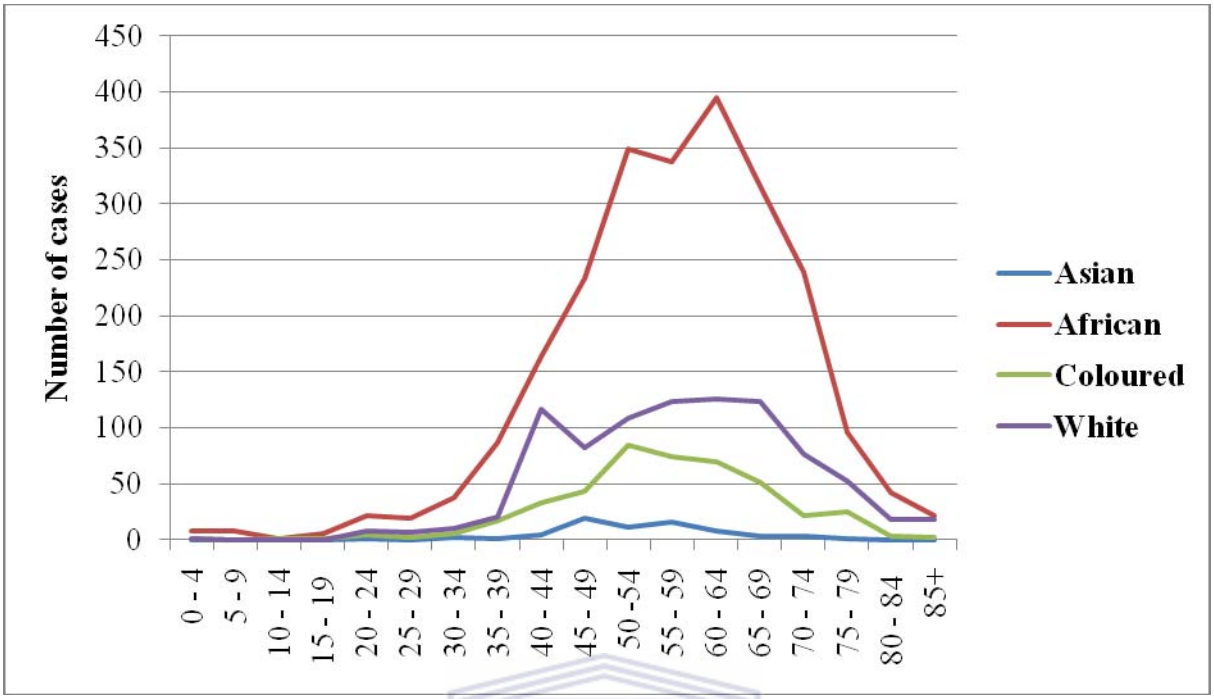
Trends of lip cancer in 10 – year age groups for white males 1988 - 1991

Appendix V



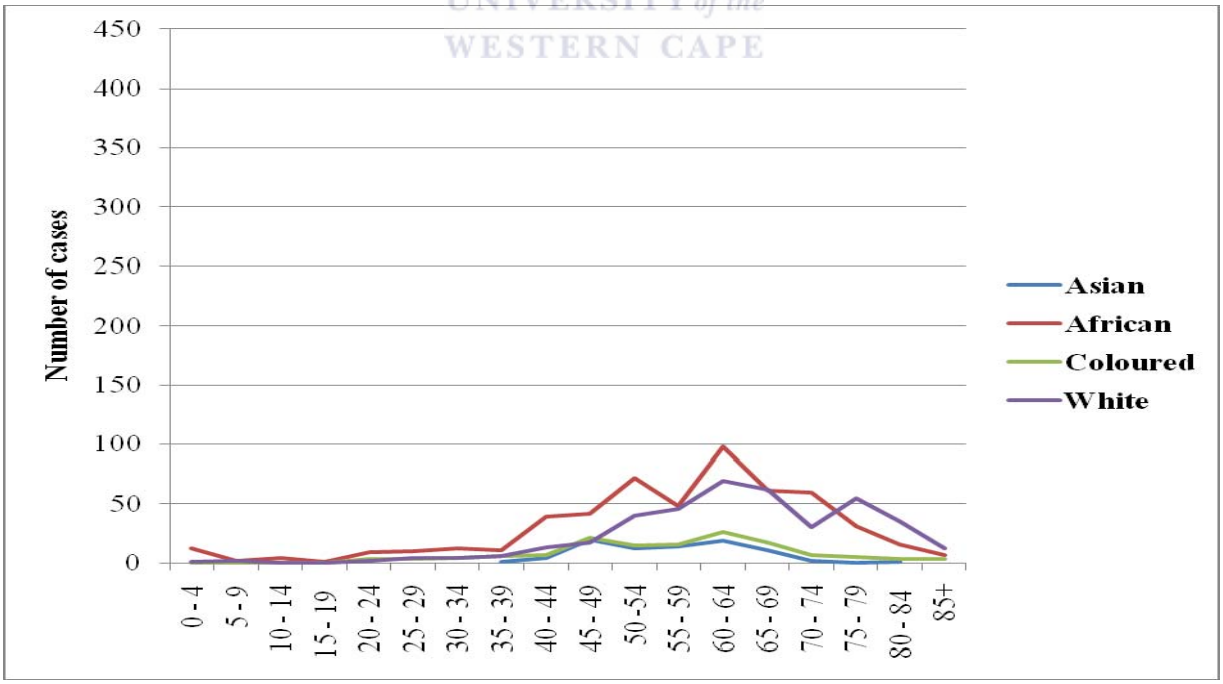
Trends of lip cancer in 10 – year age groups for white females 1988 - 1991

Appendix VI



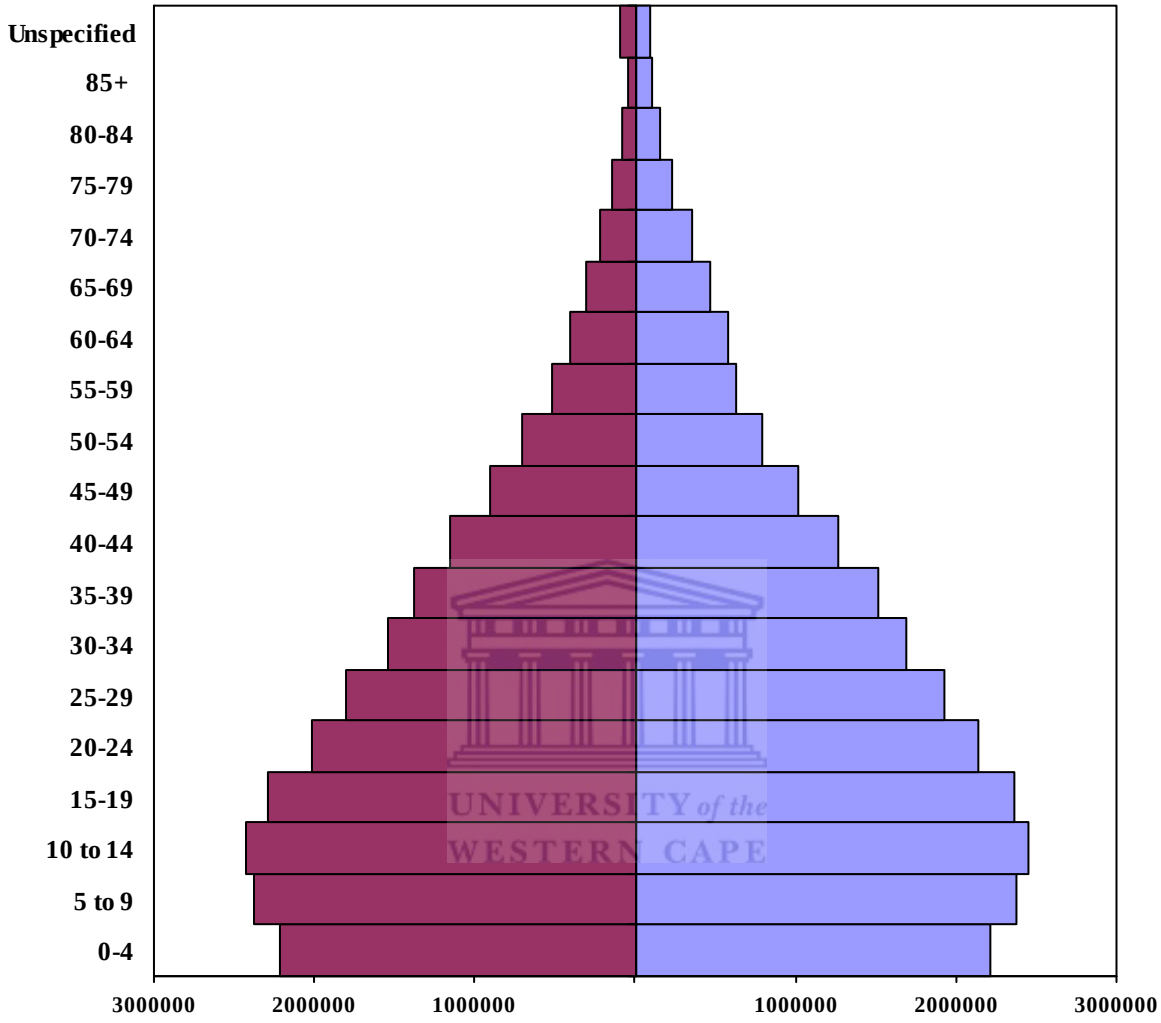
5-year age distribution of oral cancer in all males 1988 – 1991 (Hille *et al.*, 1996).

Appendix VII



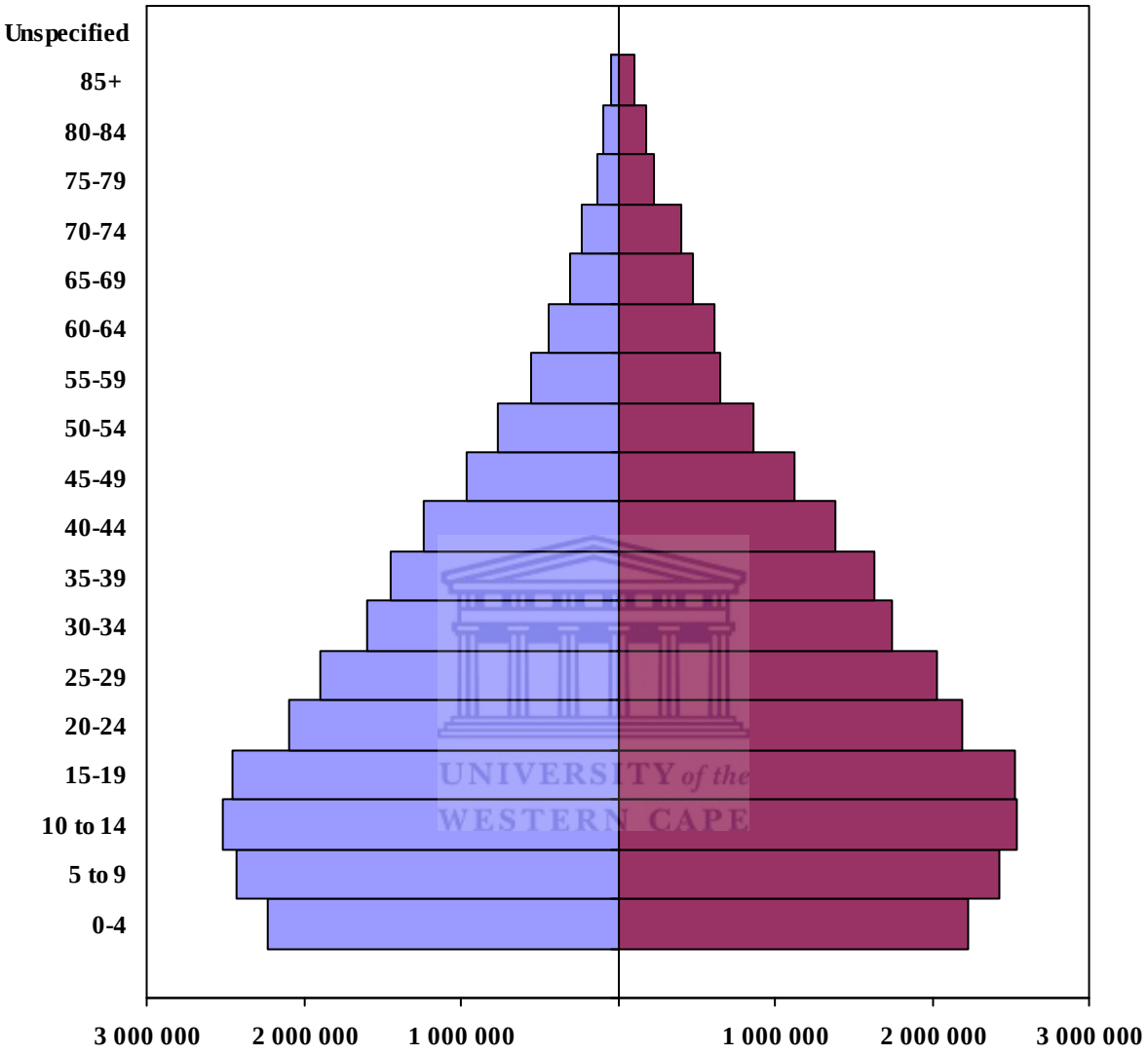
5-year age distribution of oral cancer in all females 1988 – 1991 (Hille *et al.*, 1996).

Appendix VIII



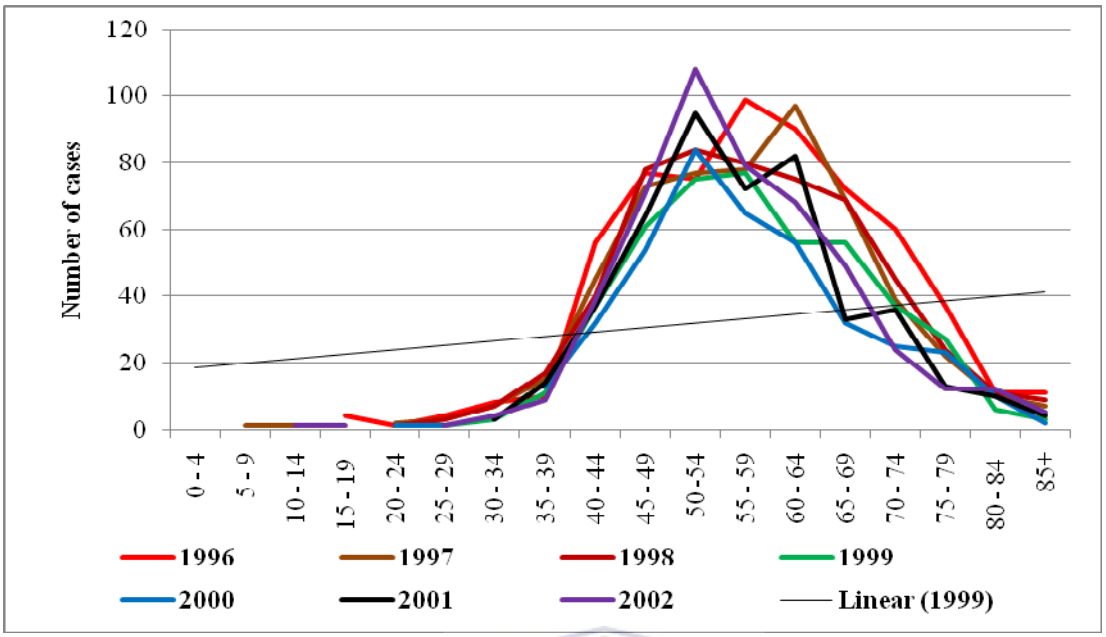
Age distribution of males and females in the total population 1999

Appendix IX

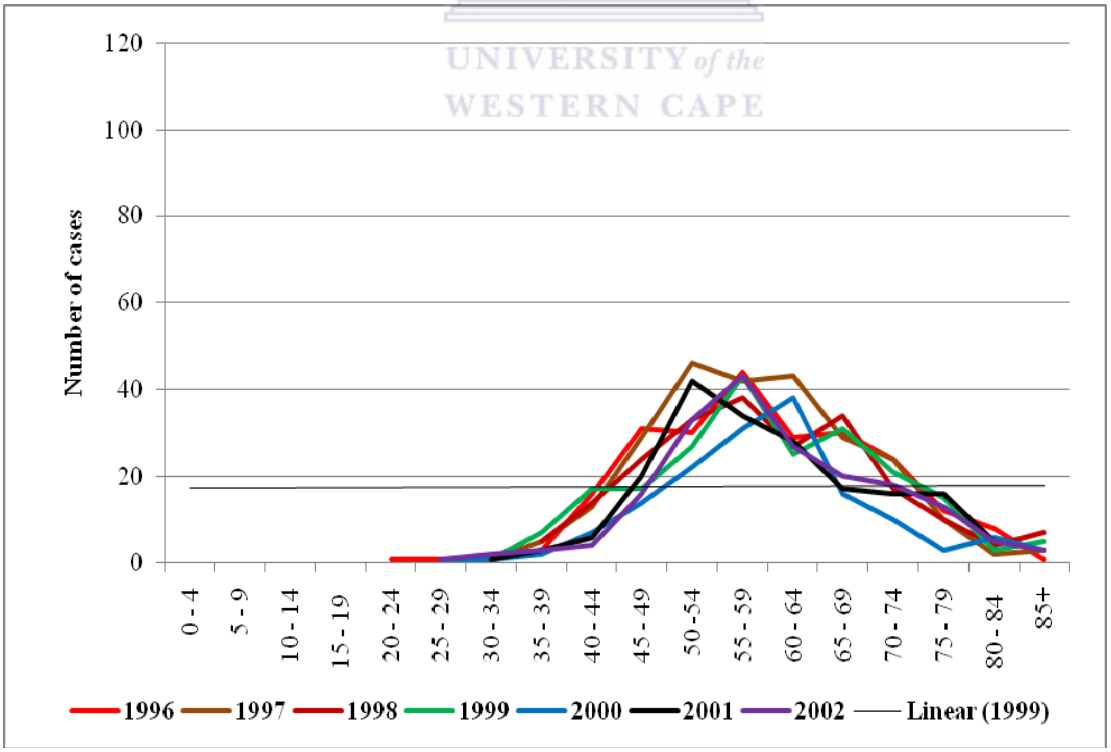


Age distribution of males and females in the total population 2001

Appendix X

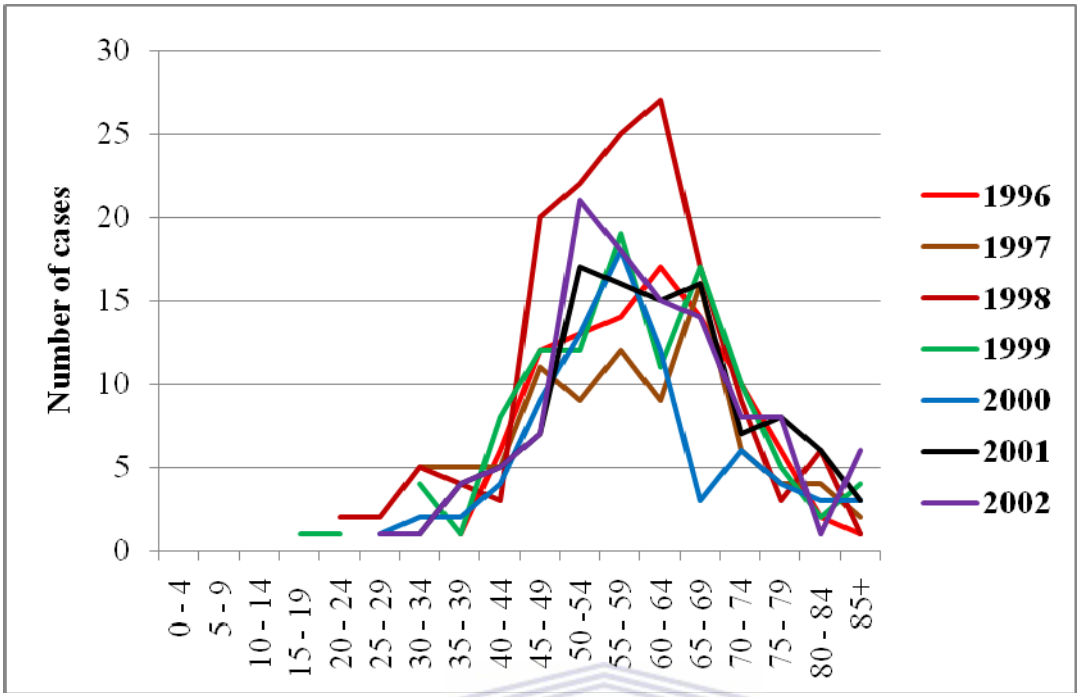


(a) Trends of oral cancer cases by 5 – year age groups for males 1996 – 2002 (Africans)

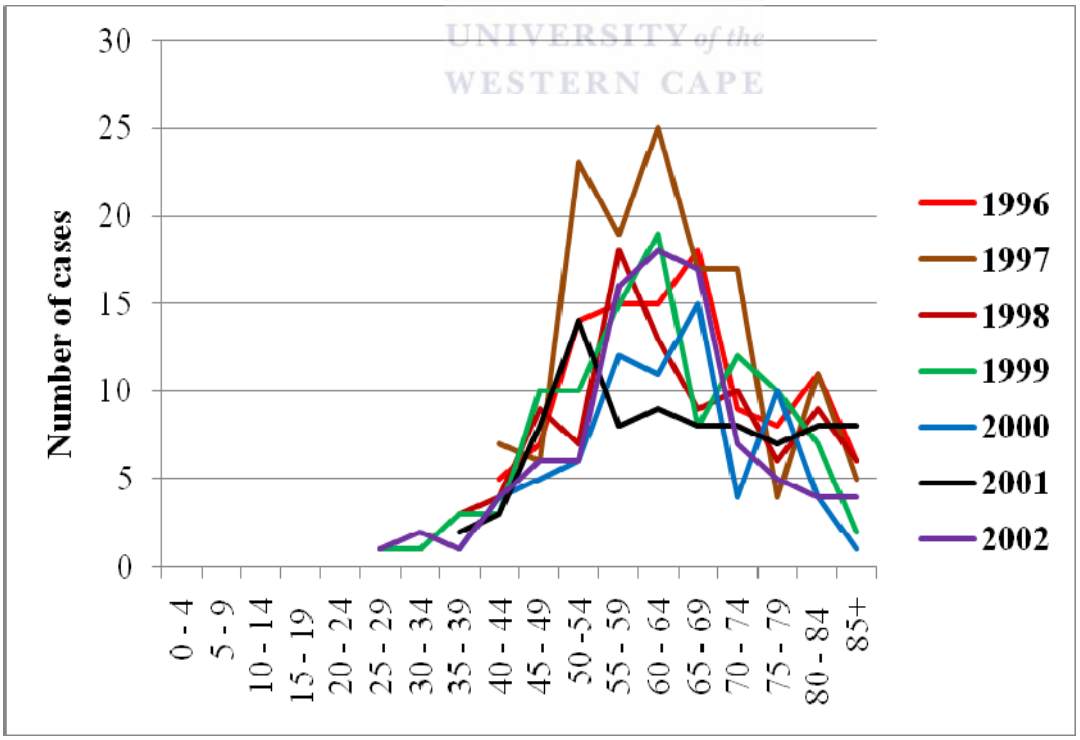


(b) Trends of oral cancer cases by 5 – year age groups for males 1996 – 2002 (White)

Appendix XI

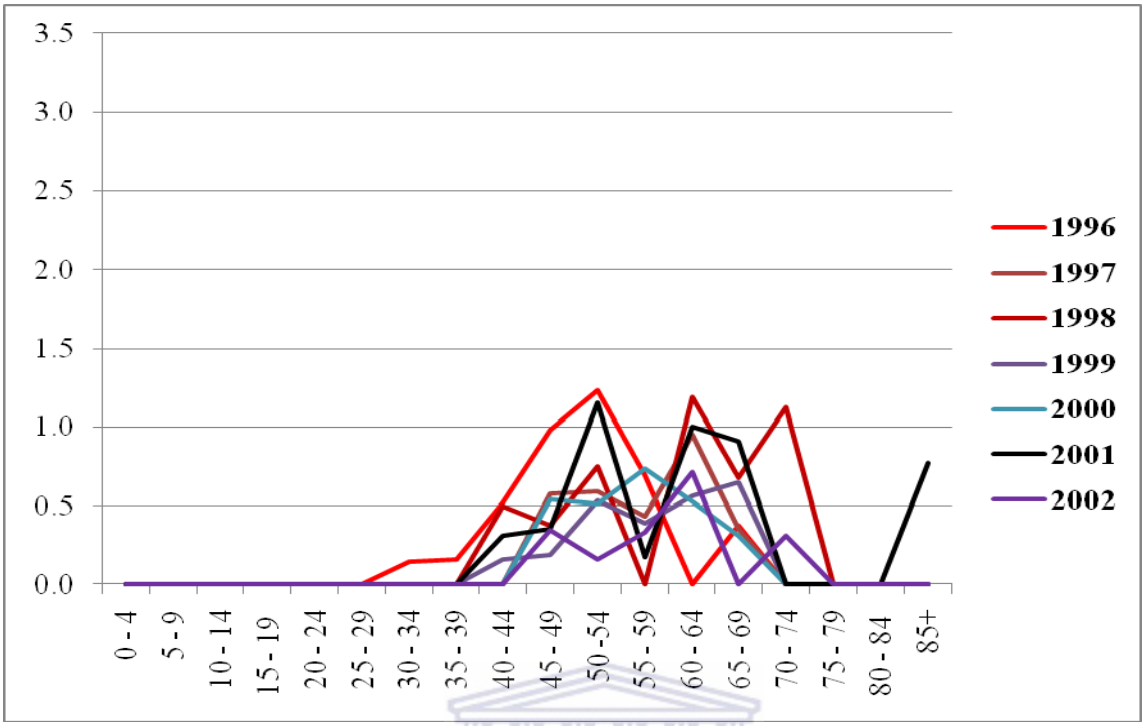


(a) Trends of oral cancer cases by 5 – year age groups for females 1996 – 2002 (Africans)

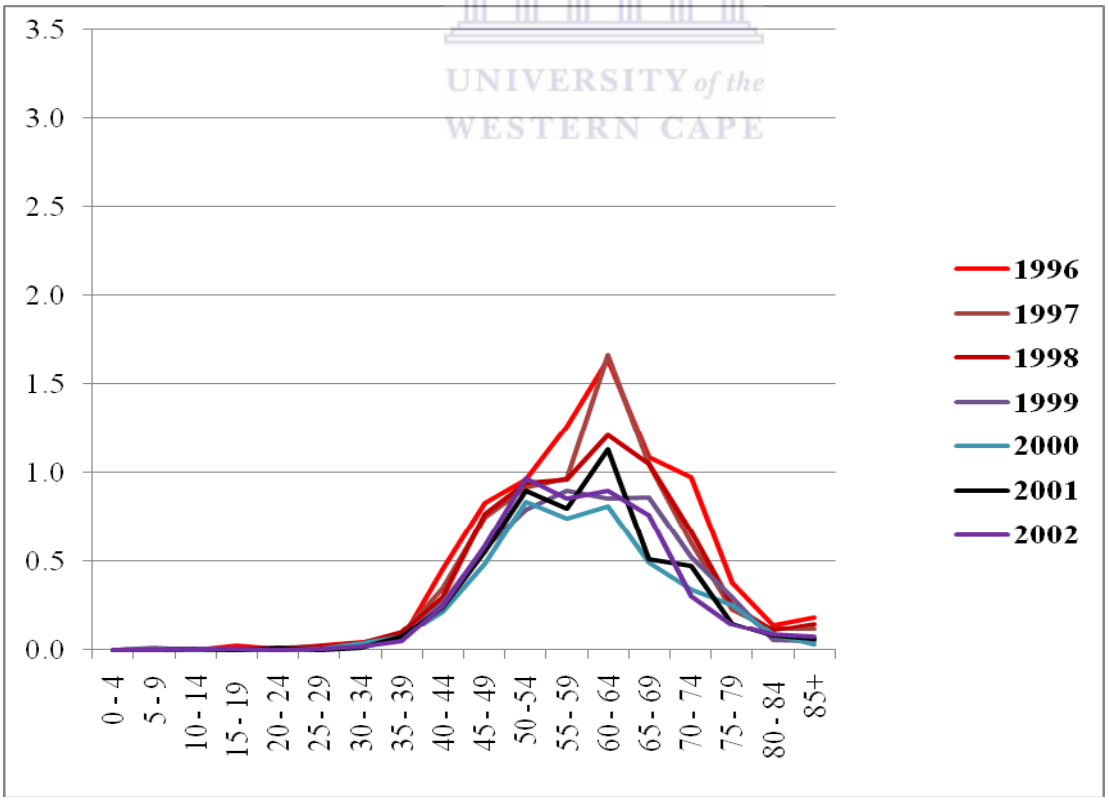


(b) Trends of oral cancer cases by 5 – year age groups for females 1996 – 2002 (Whites)

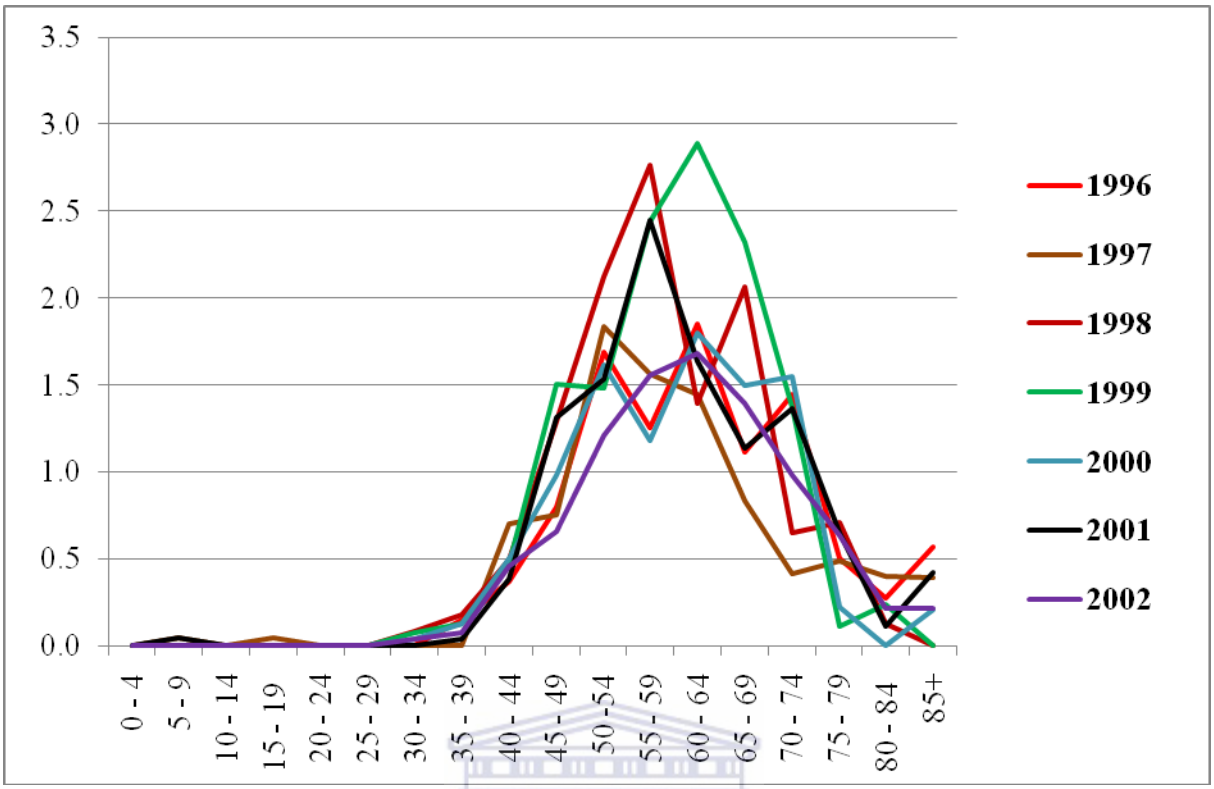
Appendix XII



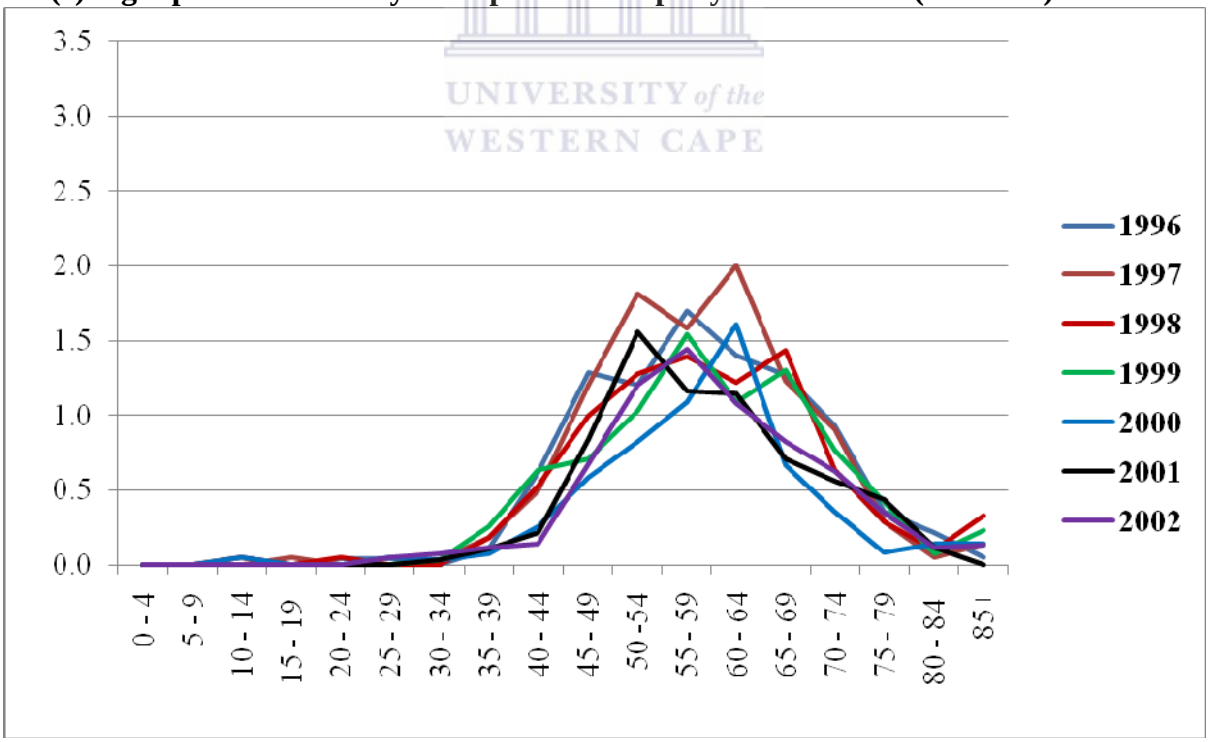
(a) Age specific morbidity rates per 100 000 per year for males (Asians)



(b)Age specific morbidity rates per 100 000 per year for males (African)

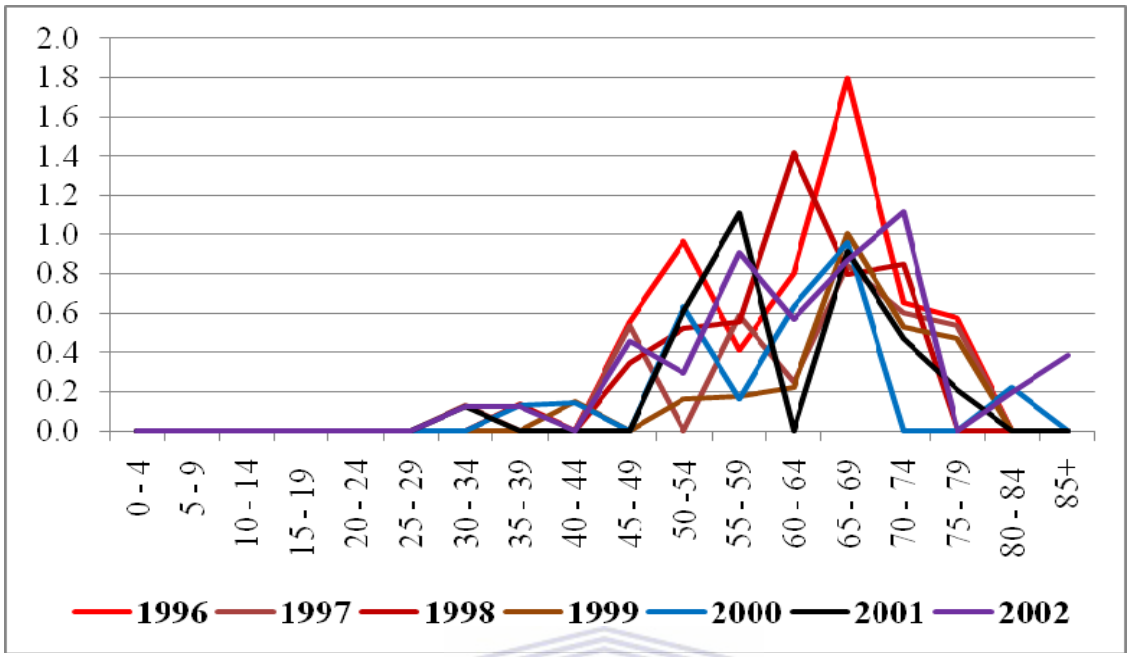


(c) Age specific morbidity rates per 100 000 per year for males (coloured)

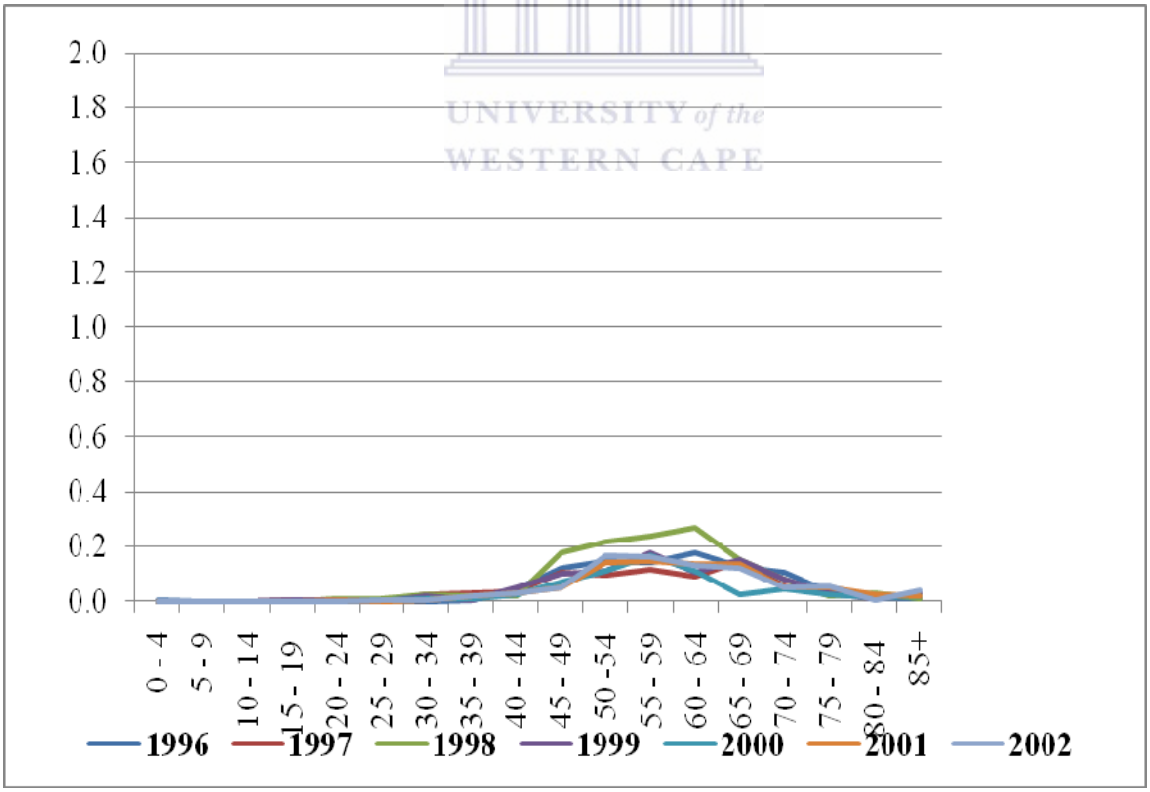


(d) Age specific morbidity rates per 100 000 per year for males (White)

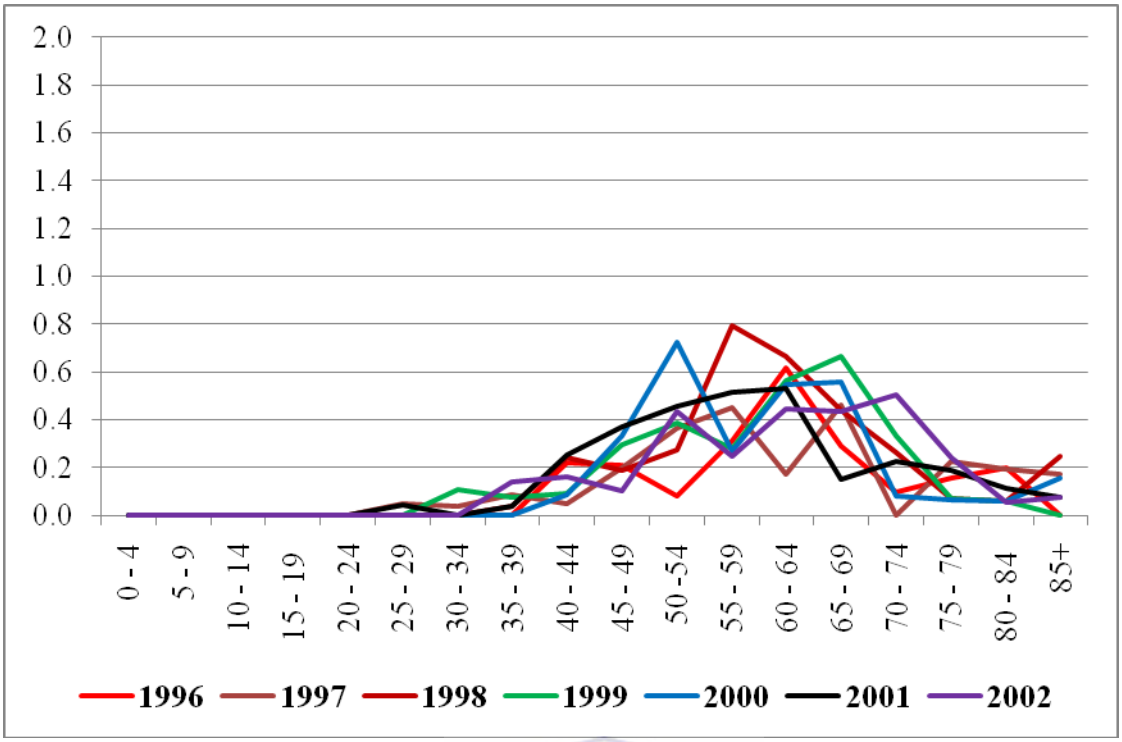
Appendix XIII



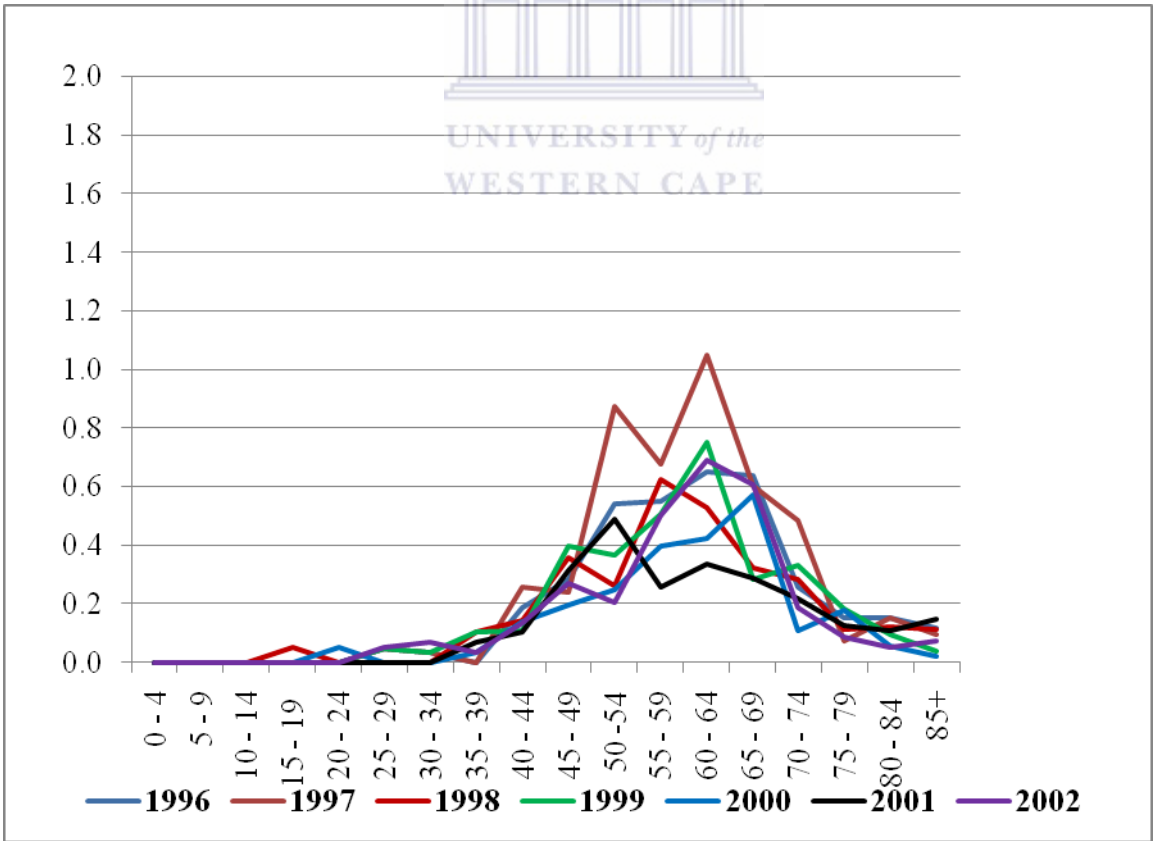
(a) Age specific morbidity rates per 100000 per year for females (Asian)



(b) Age specific morbidity rates per 100000 per year for females (African)



(c) Age specific morbidity rates per 100000 per year for females (coloured)



(d) Age specific morbidity rates per 100000 per year for females (White)

Appendix XIV

		Asian		African		Coloured		White			
		M	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**
1996 – 2002	**South Africa**	3.46	4.19	6.19	0.93	10.82	2.88	8.19	3.23		
1993 – 1995	**South Africa**	4.49	4.19	6.17	1.1	8.85	1.94	8.03	3.67		
1992 – 2004	**United States**	**Asian/Pacific Islander**		**Blacks**		**Hispanic Latino**		**Non Hispanic**		**American Indian**	
		3.6	2.1	8.6	2.7	3.8	1.8	7.1	3.3	4.2	2.4

South Africa 1993 – 1995 (Hille and Shear, 2001), USA 1992 – 2004 (Brown *et al.*,2010)

Age standardized rates per 100 000 per year for oral squamous cell carcinoma by gender and race/ethnicity

Appendix XV

Population group	**1988-1991**	**1992**	**1993-1995**	**1996-2002**
Asian male	1:161	1:435	1:167	1:188
Asian female	1:125	1:233	1:97	1:120
African male	1:86	1:99	1:122	1:92
African female	1:445	1:527	1:770	1:596
Coloured male	1:65	1:60	1:91	1:49
Coloured female	1:244	1:334	1:435	1:162
White male	1:104	1:119	1:106	1:71
White female	1:278	1:345	1:213	1:156
All male	1:91	1:92	1:115	1:83
All female	1:358	1:400	1:401	1:319

Cumulative lifetime risk for developing intraoral squamous cell carcinoma in the South African population for the periods 1996-2002 compared with the previous South African studies.

1988 – 1991 (Hille *et al.*, 1996) 1992, 1993 – 1995 (Hille and Shear, 2001)