CHAPTER 12

# LIFESTYLE-INDUCED CANCER IN SOUTH AFRICA


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## 1 INTRODUCTION

### 1.1 Global burden of cancer

Worldwide, there were approximately 10.1 million new cases, 6.2 million deaths and 22.4 million persons living with cancer in the year 2000.[1] This represents an increase of 19% in incidence and 18% in mortality since 1990, in keeping with population growth and ageing. In terms of incidence, the most common cancers worldwide (excluding non-melanoma skin cancers) are lung, (12.3% of all cancers), breast (10.4%) and colorectal (9.4%).[2] For any disease, the relationship of incidence to mortality is an indication of prognosis. As lung cancer is associated with poor prognosis, it is also the largest single cause of death from cancer in the world (17.8% of all cancer deaths). Cancer of the stomach (10.4%) and liver (8.8%) rank second and third, respectively, in terms of deaths. Differences in the distribution between the sexes are largely attributed to differences in exposure to risk factors rather than to variations in susceptibility. Generally, the relationship of incidence to mortality is not affected by sex.[2]

Although the risk of developing cancer is still higher in the developed regions of the world, the control of communicable diseases, as well as population ageing in developing countries, point to an increasing burden of cancer worldwide.[3] Pisani *et al*.[4] have projected a 30% increase in the number of cancer deaths in developed countries, and more than double this increase (71%) in developing countries from 1990 to 2010 because of demographic changes alone.

The unequal distribution of cancer burden between the developing and developed world can largely be explained by differences in the distribution of aetiological risk factors, including infectious agents and differences in lifestyle. Dietary factors are believed to be of major significance.[2] Cancer is not a rare disease in Africa. In addition to the huge load of AIDS-related Kaposi's sarcoma, the probability of developing cancer by age 65 years in a female living in Kampala or Harare is only 20% lower than that of females in Western Europe.[5] However, cancer treatment facilities in most of Africa are minimal.[5]

This chapter outlines the epidemiology and aetiology of the ten leading cancers in South Africa, with special emphasis, wherever possible, on South African research attempting to quantify the local burden of cancer and estimate the burden attributed to selected risk factors. Such studies are important in helping to better allocate resources towards the prevention and treatment of cancer. The focus will also be on research into the causes and prevention of these cancers. According to Doll and Peto[6] about 75% of cancers in the United States in 1970 could have been avoided, and more recently, Parkin *et al*.[7] estimated that there would have been 22.5% fewer cases of cancer in the developing world in 1990 if specific infections had been prevented. Lifestyle-induced cancers are likely to affect various population groups differently. Because of the diversity of cultures and lifestyles in the South African population, cancer burden, wherever possible, is reported by age, sex, and population group.

### 1.2 Cancer mortality trends

Bradshaw and Harrington[8] reviewed available mortality data for South Africa from 1949-1979 for whites, coloureds and Asians, and from 1968-1977 for Africans in urban areas. In African males, there were increases in oesophageal and lung cancer mortality while in females there was a small increase in mortality from cervix, breast and lung cancer, while stomach cancer


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declined slightly. In coloured males, there were dramatic increases in mortality from lung and oesophageal cancer over the period 1949-1979, while stomach cancer mortality declined after 1969. The rates for both cervix and breast cancer increased for coloured females over that period while the rates for stomach cancer decreased.

In white males, there was a threefold increase in lung cancer rates, while there was decrease of about the same magnitude in stomach cancer. Mortality from prostate and colorectal cancers remained stable. In white females, breast cancer mortality increased while lung cancer rates more than doubled. Colorectal cancer remained stable and mortality from cervix and stomach cancer declined. Because of the small numbers of deaths, mortality rates in the Asian population show much fluctuation from year to year. Lung cancer mortality increased over the period 1949-1979 in Asian males while breast cancer increased in females. There was a decline in mortality rates of stomach cancer in Asians of both sexes.[5]

### 1.3 Risk factor profile

The lifestyle of the urban African population, particularly in the main industrial areas of Johannesburg and Soweto, has changed dramatically over the last few decades. In terms of risk factors for cancer, there have been higher rates of smoking and alcohol consumption.[9-11] The relationship between alcohol and the emergence of a modern urban-industrial system, however, is complex as highlighted by van Onselen,[12] with the development of alcohol regulation in South Africa serving the interest of the mining industry. In the 1890s, unskilled workers were initially encouraged to consume vast quantities of alcohol and the mine owners profited from the sale of alcohol to their workers. However, after 1896, when the deep mines on the Witwatersrand went into production, the mine owners needed a sober labour force and the sale of liquor to Africans was restricted. Traditional beer (home and commercially brewed using local recipes) became the main type of alcohol used.[10] Then in 1962, legislation that made it illegal for Africans to purchase 'western spirits' was repealed, and since then there has been a marked increase in their consumption.[10]

In addition to these leading risk factors associated with a western lifestyle, other risk factors associated with poverty and underdevelopment, such as poor nutrition and exposure to indoor smoke from solid fuels, still persist and are responsible for significant increases in some cancers. Unsafe sex and associated infection with sexually transmitted infections, including HIV, is one of the leading causes of disease burden in South Africa and increases in some cancers can be attributed to this important risk factor.

The current mortality pattern of chronic diseases reflects a lifetime of exposure to unhealthy lifestyles. Unhealthy lifestyles in our society are steadily given up by the wealthy and taken up among the poor, who, as they age, are placed at risk for these chronic diseases.[13] Although cancer is a leading cause of death in all communities in South Africa, the types of cancer differ between poor and rich areas. Oesophageal cancer is by far the most common cause of premature mortality for males in poor areas, followed by lung cancer and liver cancer. For males in rich areas, lung cancer is the most common followed by oesophageal cancer and leukaemia. Cervical cancer is the most common cause of premature mortality for females in poor areas, followed by oesophageal cancer and breast cancer. In rich areas, breast cancer is the most common cause of premature mortality followed by cervical cancer and lung cancer.[14]

## 2 BURDEN OF LIFESTYLE-INDUCED CANCERS IN SOUTH AFRICA

### 2.1 The South African National Burden of Disease study

Initial estimates from the South African National Burden of Disease study (SA NBD)[15] were recently revised using more recent data.[16] Revised estimates show that in the year 2000, all cancers as a group (this disease category is also referred to as the malignant neoplasms category) accounted for 41 657 (8.0% of all) deaths and were ranked as the fourth leading cause of death for all persons. Among older (60+ years) persons, cancers as a group ranked second to cardiovascular disease and accounted for 15.3% of all deaths.[15] The top 20 causes of cancer deaths for South Africa in 2000 were ranked for males, females, and persons by percentage of all cancer deaths and the results are presented in Table 12.1.

The aero-digestive cancers (trachea/bronchi/lung and oesophageal cancers) were the leading causes of cancer deaths in South Africa. In males, trachea/bronchi/lung (referred to as lung) cancer accounted for 21.9% of all cancer deaths, followed by oesophageal cancer (16.7% of cancer deaths) and prostate cancer (11.8%). Cancer of the cervix (17.2%), breast (15.6%) and lung (10.9%) were among the top causes of cancer deaths in females (Table 12.1). For most cancers including lung, oesophageal, stomach and liver, cancer deaths were higher among males than females (Fig. 1). Age-standardised (to the world population)[17] mortality rates/100 000 for each cancer by sex and population group for South Africa 2000 are presented in Table 12.2. The age-standardised all-cancer death rate of 148.6 per 100 000 for persons for South Africa 2000 is compared with other countries in Fig. 2. South Africa ranks high with rates similar to those in developed countries such as England and Wales, although the pattern of cancers is different (this is described in more detail in the epidemiology sections). Age-specific death rates for males and females are presented in Figs. 3 and 4. It is interesting to note that death rates for trachea/bronchi/lung and oesophageal cancer in males begin to increase from the relatively younger age group of 35-44 years. In females, death rates for breast and cervical cancer begin to increase from the 25-34-year age group.

Table 12.1. Percentage of cancer deaths by cause, South Africa 2000

| Persons | | | Males | | | Females | | |
|---|---|---|---|---|---|---|---|---|
| Rank | Cause of death | % | Rank | Cause of death | % | Rank | Cause of death | % |
| 1 | Trachea/bronchi/ lung cancer | 16.5 | 1 | Trachea/bronchi/ lung cancer | 21.9 | 1 | Cervix cancer | 17.2 |
| 2 | Oesophageal cancer | 13.4 | 2 | Oesophageal cancer | 16.7 | 2 | Breast cancer | 15.6 |
| 3 | Cervix cancer | 8.4 | 3 | Prostate cancer | 11.8 | 3 | Trachea/bronchi/ lung cancer | 10.9 |
| 4 | Breast cancer | 7.7 | 4 | Liver cancer | 7.8 | 4 | Oesophageal cancer | 9.9 |
| 5 | Liver cancer | 6.4 | 5 | Stomach cancer | 6.5 | 5 | Colorectal cancer | 6.9 |
| 6 | Colorectal cancer | 6.2 | 6 | Colorectal cancer | 5.4 | 6 | Liver cancer | 4.9 |
| 7 | Prostate cancer | 6.1 | 7 | Mouth and oropharynx | 4.6 | 7 | Stomach cancer | 4.7 |
| 8 | Stomach cancer | 5.6 | 8 | Leukaemia | 3.8 | 8 | Pancreas cancer | 3.7 |
| 9 | Pancreas cancer | 3.7 | 9 | Pancreas cancer | 3.7 | 9 | Ovary cancer | 3.5 |
| 10 | Leukaemia | 3.5 | 10 | Larynx cancer | 3.0 | 10 | Leukaemia | 3.2 |
| 11 | Mouth and oropharynx | 3.3 | 11 | Lymphoma | 2.8 | 11 | Corpus uteri cancer | 3.1 |
| 12 | Lymphoma | 2.5 | 12 | Bladder cancer | 2.2 | 12 | Lymphoma | 2.1 |
| 13 | Larynx cancer | 1.8 | 13 | Bone and connective tissue cancer | 1.7 | 13 | Mouth and oropharynx | 2.0 |
| 14 | Ovary cancer | 1.7 | 14 | Brain cancer | 1.3 | 14 | Bone and connective tissue cancer | 1.6 |
| 15 | Bone and connective tissue cancer | 1.7 | 15 | Kidney cancer | 1.2 | 15 | Brain cancer | 1.2 |
| 16 | Bladder cancer | 1.6 | 16 | Melanoma | 1.1 | 16 | Bladder cancer | 1.0 |
| 17 | Corpus uteri cancer | 1.5 | 17 | Non-melanoma skin cancers | 0.7 | 17 | Melanoma | 1.0 |
| 18 | Brain cancer | 1.3 | 18 | Breast cancer | 0.2 | 18 | Kidney cancer | 0.9 |
| 19 | Melanoma | 1.0 | 19 | | | 19 | Larynx cancer | 0.6 |
| 20 | Kidney cancer | 1.0 | 20 | | | 20 | Non-melanoma skin cancers | 0.5 |
| 21 | Non-melanoma skin cancers | 0.6 | 21 | | | 21 | | |
| | All cancers | 100.0 | | All cancers | 100.0 | | All cancers | 100.0 |

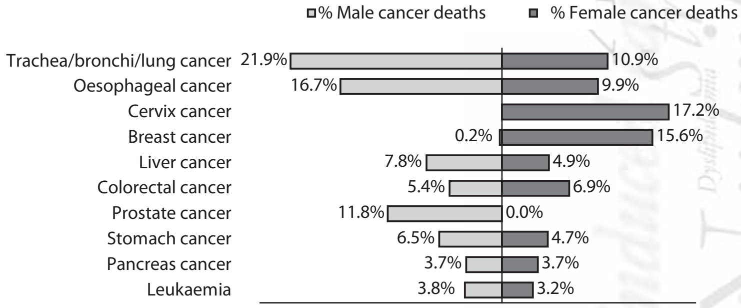


Figure 1: Percentage distribution of the top ten causes of cancer deaths by sex, South Africa, 2000[16]

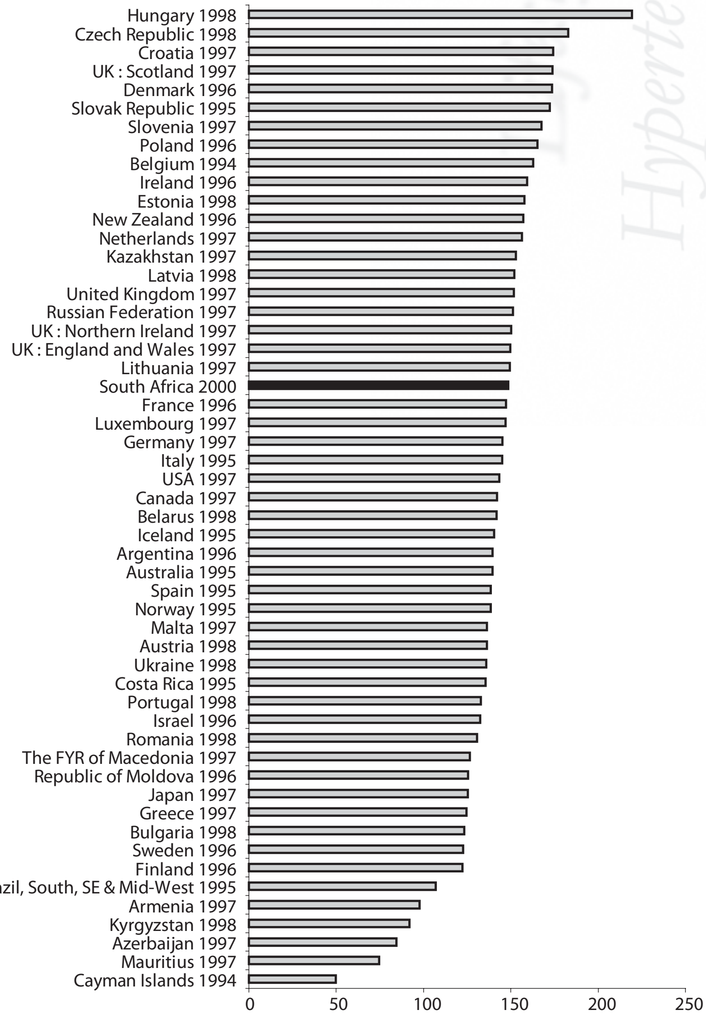


Figure 2: International comparisons for malignant neoplasms age-standardised (to the world population) rates/100 000[17] (South African data have been adjusted, whereas only raw data are available from certain countries)

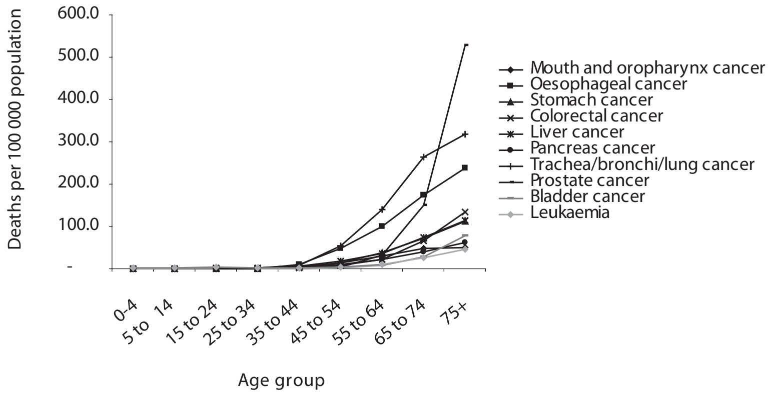


Figure 3: Male age-specific cancer deaths rates, South Africa 2000[16]

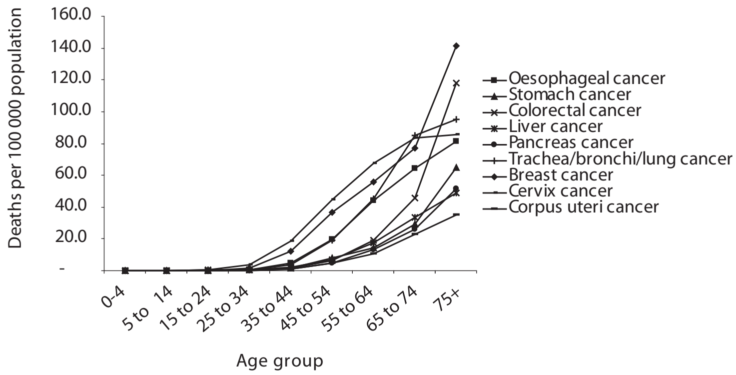


Figure 4: Female age-specific cancer deaths rates, South Africa 2000[16]

## 2.2 Population group differences in mortality profile

Population group estimates of the revised SA NBD study indicate that the highest age-standardised cancer death rates are found in the coloured population (212.5/100 000), followed by the white (198.9), African (126.0) and Asian (121.4) groups (Fig. 5 and Table 12.2). The coloured population had the highest rates for cancer of the lung (54.6) and stomach (19.3). White males had the highest prostate (41.1) and colorectal (24.3) cancer death rates. The breast cancer age-standardised death rate was highest in white females (35.2). The African population had the highest death rates from cervical cancer (26.9) in females and oesophageal cancer in males (41.4) and females (17.6).

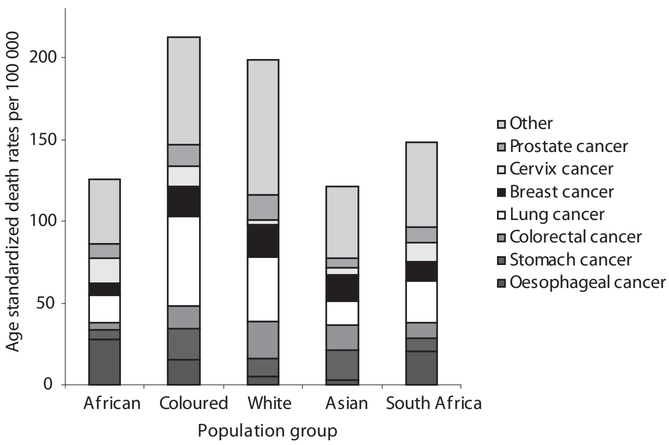


Figure 5: Population group estimates of age-standardised (to the world population) cancer death rates, 2000[16]

Age-specific death rates for males and females by population group for the most important cancers are shown in Figs. 6 (a and b) and 7. For lung cancer, age-specific death rates were also plotted on a logarithmic scale for ages 35 years and older (Fig. 6b). The rapid increase in the rate of prostate cancer in older ages (Fig. 3) reflects the pattern seen in white males (Fig. 7). In some cases, particularly noticeable for cervical cancer in coloured females and lung cancer in coloured males, the age distribution follows an "S" shape rather than a steep or progressive increase with age. This "S" shape is indicative of an exposure to risk factors being introduced at a certain age resulting in a more sudden increase with age. Provincial and population group differences, as well as age and gender patterns, will be discussed in more detail in the epidemiology section of the specific cancers.

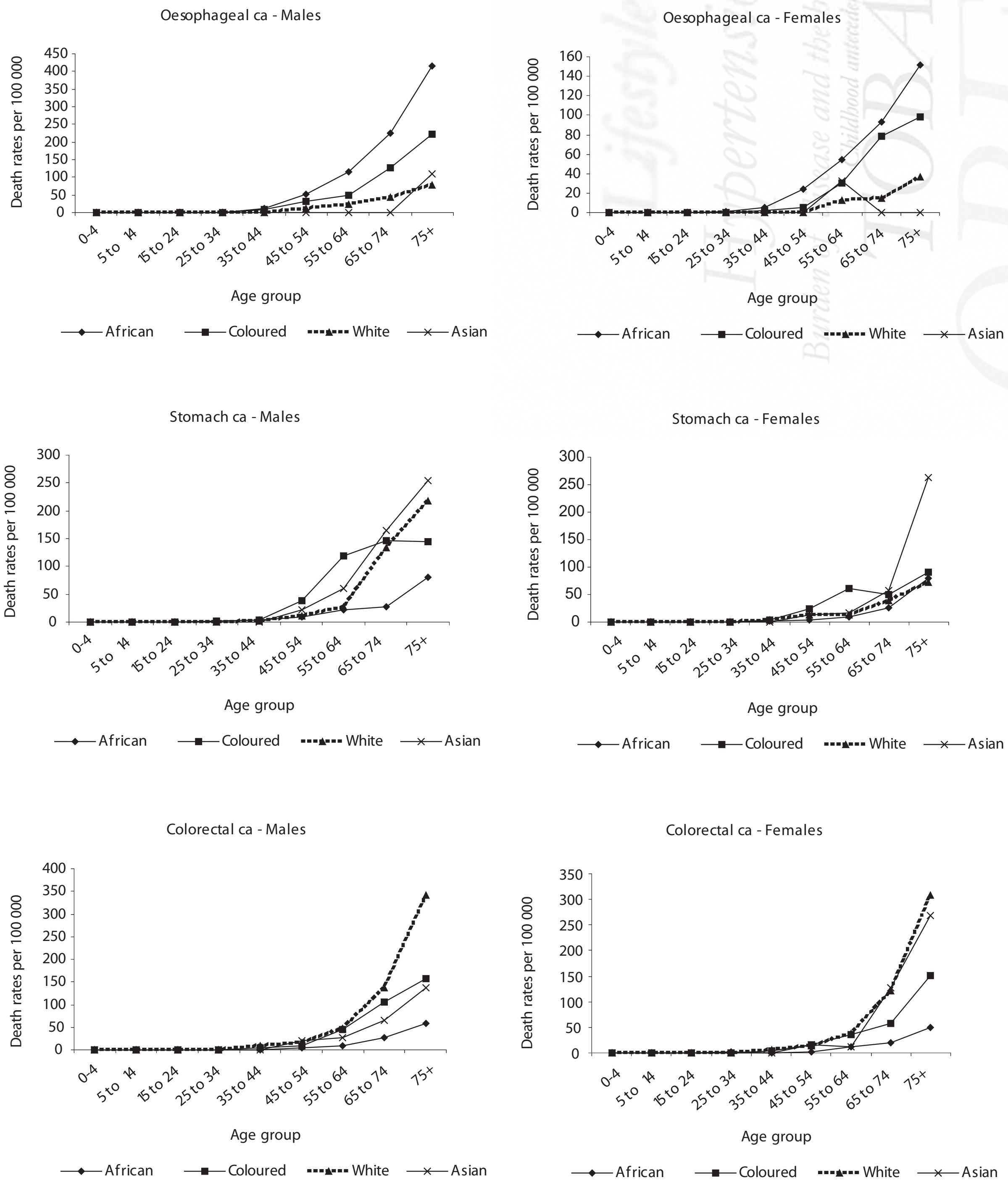


Figure 6a: Age-specific death rates for selected cancers by sex and population group, South Africa 2000[16] (Asian female rates are unstable because of small numbers)

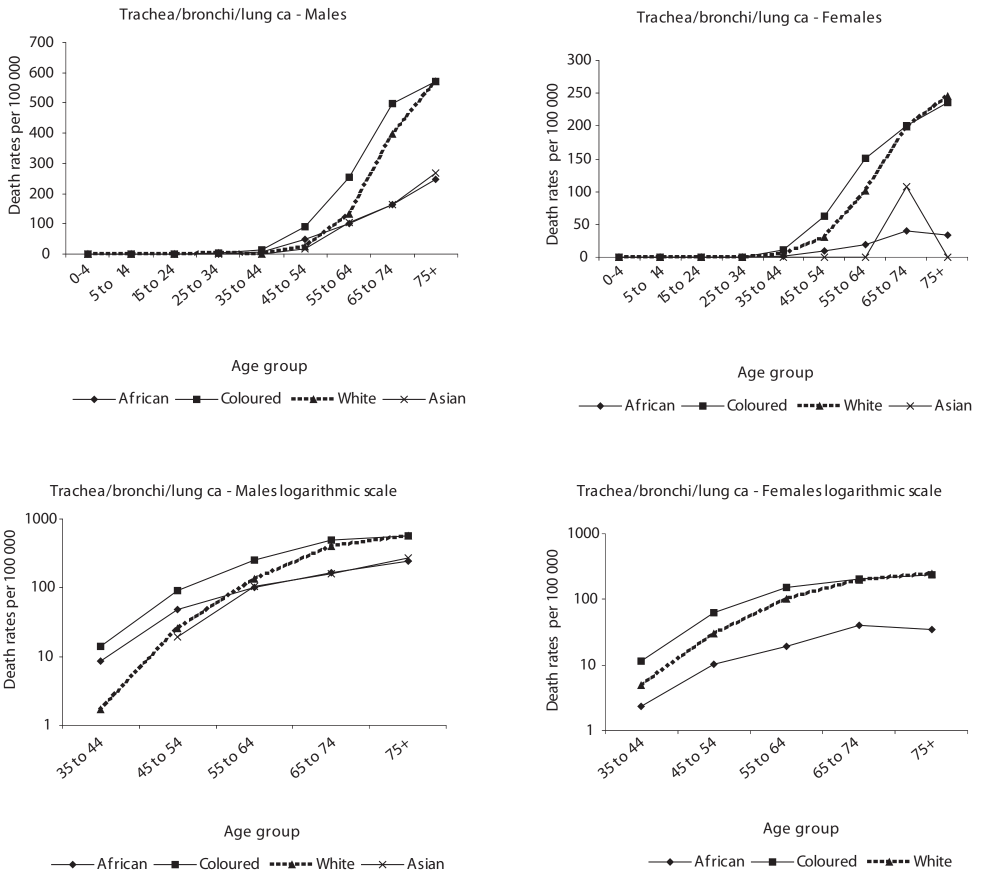


Figure 6b: Age-specific death rates for lung cancer by sex and population group, South Africa 2000[16] (Asian female rates were excluded from log scales because of small numbers)

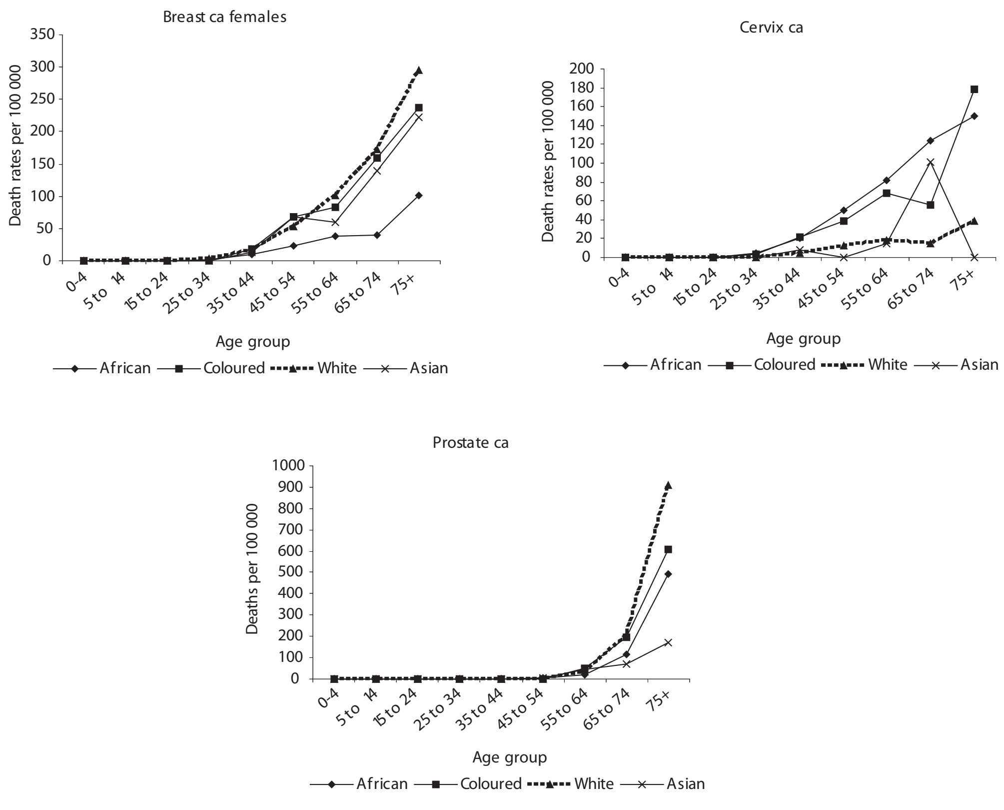


Figure 7: Age-specific death rates for selected cancers by population group, South Africa 2000[16] (Asian female rates are unstable because of small numbers)

Table 12.2. Age-standardised (to the world population) death rates per 100 000 by sex and population group, South Africa 2000[16]

| | African | | | Coloured | | | White | | | Asian | | | South Africa | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Cancer site | Males | Females | Persons | Males | Females | Persons | Males | Females | Persons | Males | Females | Persons | Males | Females | Persons |
| Mouth and oropharynx | 7.7 | 2.4 | 4.7 | 17.3 | 4.4 | 9.8 | 6.7 | 2.6 | 4.4 | 0.9 | 5.2 | 3.3 | 8.5 | 2.5 | 5.0 |
| Oesophagus | 41.4 | 17.6 | 27.6 | 22.0 | 10.4 | 15.2 | 7.7 | 3.0 | 5.0 | 3.3 | 2.6 | 2.7 | 31.6 | 12.4 | 20.2 |
| Stomach | 7.4 | 5.2 | 6.2 | 27.0 | 13.6 | 19.3 | 17.3 | 7.3 | 11.3 | 23.7 | 13.8 | 18.2 | 12.5 | 5.9 | 8.5 |
| Colorectum | 4.7 | 4.1 | 4.3 | 15.3 | 12.6 | 13.7 | 24.3 | 21.2 | 22.6 | 12.0 | 17.4 | 15.3 | 10.8 | 8.6 | 9.5 |
| Liver | 16.3 | 6.6 | 10.7 | 9.1 | 8.6 | 8.6 | 7.8 | 5.1 | 6.2 | 7.7 | 6.5 | 7.1 | 14.0 | 6.0 | 9.3 |
| Pancreas | 4.6 | 2.6 | 3.5 | 9.1 | 8.7 | 9.0 | 12.9 | 10.2 | 11.5 | 3.0 | 5.4 | 4.4 | 7.2 | 4.7 | 5.7 |
| Larynx | 4.9 | 0.6 | 2.5 | 10.2 | 1.9 | 5.4 | 4.1 | 0.5 | 2.0 | 11.5 | 0.0 | 4.6 | 5.7 | 0.7 | 2.7 |
| Trachea/bronchi/lung | 31.1 | 6.3 | 16.9 | 77.1 | 38.8 | 54.6 | 52.3 | 30.1 | 39.1 | 27.5 | 5.6 | 15.1 | 42.3 | 13.8 | 25.3 |
| Bone and connective tissue | 1.6 | 1.3 | 1.5 | 2.6 | 4.7 | 3.9 | 3.9 | 2.0 | 2.9 | 1.9 | 0.0 | 0.8 | 2.4 | 1.8 | 2.1 |
| Melanoma | 0.4 | 0.1 | 0.2 | 0.9 | 0.5 | 0.6 | 6.6 | 4.8 | 5.7 | 0.0 | 0.0 | 0.0 | 2.0 | 1.2 | 1.6 |
| Non-melanoma skin | 0.6 | 0.5 | 0.6 | 2.2 | 0.0 | 1.0 | 1.8 | 0.7 | 1.2 | 0.0 | 0.8 | 0.4 | 1.2 | 0.6 | 0.9 |
| Breast | 0.3 | 12.7 | 7.3 | 0.0 | 32.7 | 18.7 | 0.0 | 35.2 | 19.5 | 0.4 | 28.5 | 16.0 | 0.5 | 19.0 | 11.3 |
| Cervix | 0.0 | 26.9 | 15.0 | 0.0 | 21.7 | 12.4 | 0.0 | 5.5 | 3.0 | 0.0 | 7.6 | 4.3 | 0.0 | 20.8 | 11.9 |
| Corpus uteri | 0.0 | 4.6 | 2.6 | 0.0 | 5.5 | 3.3 | 0.0 | 2.6 | 1.6 | 0.0 | 1.9 | 1.1 | 0.0 | 3.9 | 2.3 |
| Ovary | 0.0 | 2.7 | 1.5 | 0.0 | 1.7 | 1.0 | 0.0 | 10.2 | 5.6 | 0.0 | 6.5 | 3.5 | 0.0 | 4.3 | 2.5 |
| Prostate | 22.9 | 0.0 | 9.0 | 33.2 | 0.0 | 12.7 | 41.1 | 0.0 | 15.7 | 13.2 | 0.0 | 5.6 | 26.8 | 0.0 | 9.8 |
| Bladder | 2.4 | 0.8 | 1.4 | 9.6 | 2.2 | 5.1 | 8.7 | 2.4 | 4.8 | 4.0 | 0.0 | 1.7 | 4.7 | 1.2 | 2.5 |
| Kidney | 0.6 | 0.3 | 0.5 | 3.1 | 1.3 | 2.1 | 4.5 | 2.6 | 3.4 | 3.3 | 0.0 | 1.4 | 2.1 | 1.0 | 1.4 |
| Brain | 1.0 | 0.4 | 0.7 | 0.5 | 1.1 | 0.8 | 5.3 | 5.4 | 5.3 | 0.0 | 1.4 | 0.8 | 2.1 | 1.5 | 1.7 |
| Lymphoma | 2.8 | 1.5 | 2.1 | 4.5 | 3.6 | 4.0 | 6.8 | 5.2 | 5.8 | 7.7 | 2.4 | 5.0 | 4.4 | 2.5 | 3.3 |
| Leukaemia | 3.2 | 2.0 | 2.6 | 4.0 | 3.2 | 3.4 | 12.2 | 7.1 | 9.4 | 3.9 | 9.6 | 6.8 | 5.7 | 3.5 | 4.4 |
| Other cancers | 4.4 | 4.6 | 4.5 | 5.8 | 9.3 | 7.8 | 11.8 | 14.2 | 13.1 | 7.0 | 0.0 | 3.1 | 6.6 | 6.6 | 6.6 |
| Malignant neoplasms | 158.2 | 103.8 | 126.0 | 253.3 | 186.5 | 212.5 | 236.0 | 177.9 | 198.9 | 131.0 | 115.3 | 121.4 | 191.0 | 122.4 | 148.6 |

## 2.3 Provincial differences in mortality profile

Estimates of provincial cancer death rates[18] are shown in Fig. 8. The Western Cape had the highest cancer death rates followed by Gauteng, the Northern Cape and the Eastern Cape provinces. The lowest rates were found in KwaZulu-Natal (KZN), Limpopo and Mpumalanga. The profile of the type of cancer also differed enormously across the provinces. The lung cancer rate among males in the more developed province of the Western Cape was extremely high. Prostate cancer was highest in the Northern Cape, followed by Free State, Gauteng, and Mpumalanga (Fig. 9). The Eastern Cape had particularly high rates of oesophageal cancer, as did males in the North West province. Nationally, cervical cancer and breast cancer death rates were at similar levels. However, there were provincial variations in the pattern of these cancers. The Western Cape had much higher breast cancer rates, while the poorer and more rural provinces of Mpumalanga, Limpopo, and the Eastern Cape had much higher cervical cancer rates (Fig. 9). It should be noted that the national average in the provincial study is slightly higher than the revised SA NBD estimates.[16]

The variations between the provinces may be related to levels of wealth and development, population group differences and demographic features of the province, geographical differences and environmental exposures, as well as access to health services or other basic services. The average profile of a province, furthermore, obscures the variability within a province. Studies comparing the mortality experienced by the different population groups, social classes and ethnic groups and for small areas may provide useful insight into the factors associated with the variations in health outcomes.[18]

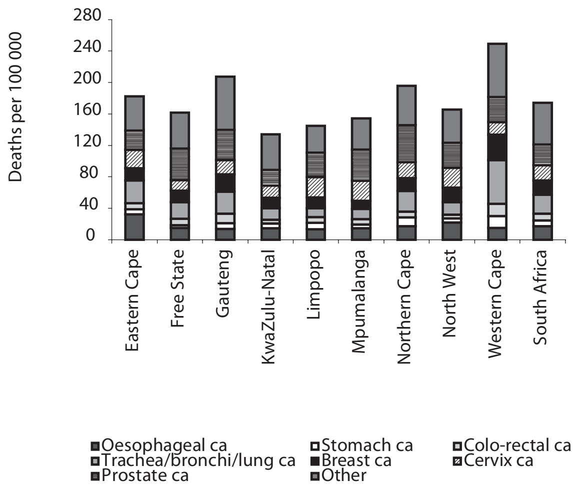


Figure 8: Provincial estimates of age-standardised cancer death rates, 2000[18]

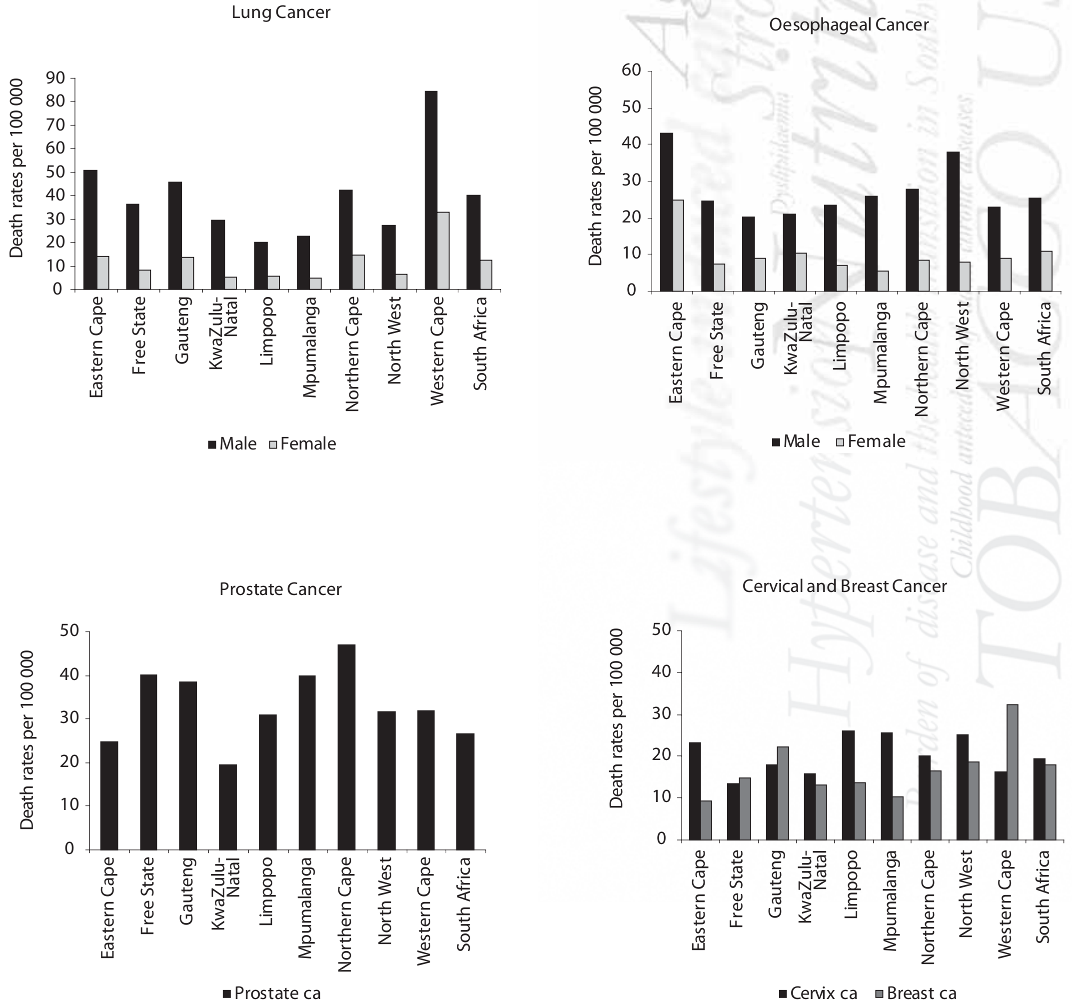


Figure 9: Provincial estimates of age-standardised death rates caused by selected cancers by sex, 2000[18]

## 2.4 Cancer incidence data for South Africa

### *2.4.1 The National Cancer Registry*

In 1986, a national, pathology-based cancer registry was established at the South African Institute for Medical Research (now the National Health Laboratory Service) as a collaborative venture with the Cancer Association of South Africa (CANSA) and the Department of Health. The National Cancer Registry (NCR) is a voluntary national cancer surveillance system. Cancer data are collected from both public and private pathology laboratories nationally, and it is the only source of national cancer incidence data, albeit the rates reported are an underestimate of the true burden. Only incident cases of primary invasive cancer diagnosed by histology, cytology or haematology are recorded.

The main objectives of the NCR are to monitor cancer burden and to publish and report cancer incidence for every year, stratifying by sex, age and population group. The NCR also attempts to report time trends. Every year approximately 80 000 cases of cancer are reported to the NCR of which about 60 000 are new cases. In 1998 and 1999, 60 172 and 60 343, respectively, new cancer cases were reported to the NCR.[19] The bulk of these were diagnosed and reported by laboratories in Gauteng (40.8% of new cases), which also has the highest number of cancer-diagnosing facilities, then KZN (18.6%) and the Western Cape (17.9%). This reflects the unequal distribution of cancer diagnostic facilities in South Africa and the movement of cancer patients seeking treatment in neighbouring provinces, as well as the transfer of specimens for testing to the more developed provinces. Missing information on population groups remains a major concern. Hot-deck imputation methods have been developed in an attempt to provide some continuity in population specific rates.[19] Male (29 428) and female (30 480) cancers comprised 50.5% and 48.8%, respectively, of all cancers in 1999, where sex was known, similar to the numbers and proportions in 1998.

Overall, the white population comprised the highest proportion of all cancer cases: 45.2% and 46.4% in 1998 and 1999, respectively (including basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) of the skin). The black population comprised the second highest proportion of new cases (39.4%, 36.8%), followed by the coloured population (8.3%, 9.1%), while the Asian population had the lowest number of reported new cases (2.3%, 2.1%).

Childhood (age 0-14 years) cancers comprised about 1% and 2% of all female and male cancers, respectively, reported for both 1998 and 1999. The top four childhood cancers in males were leukaemia, brain, kidney and non-Hodgkin lymphoma, while in females it was leukaemia, kidney, brain and bone.[19]

The frequency distribution of the top ten cancers for the two years 1998-99 and all ages is shown in Fig. 10. Breast and cervix cancers and BCC comprised more than half of all the female cancers reported in 1998 and 1999. In males, BCC (23.3%) and prostate (13.6%) cancers remained the first and second most common cancers.

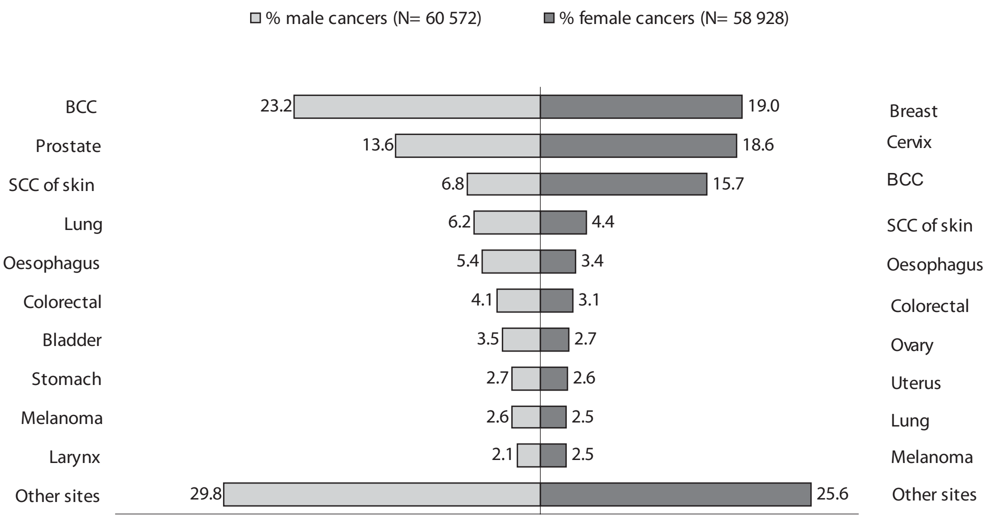


Figure 10: Percentage distribution of 10 most common cancers reported to NCR by sex, South Africa 1998 and 1999[19]
BCC Basal cell carcinoma
SCC Squamous cell carcinoma

BCC and SCC of skin are the most prevalent neoplasms, particularly among the white population group, and tend to overshadow all other cancer sites. Consequently, the common practice internationally is to exclude BCC and SCC of skin from the calculations of total cancer rates, and therefore all incidence rates and rankings reported in this chapter, exclude these two cancers. Table 12.3 presents a summary of the five leading cancers diagnosed in 1998 and 1999 for each population group in males and females. In South Africa, 1 in 4 males and 1 in 5 females (aged 0-74 years) were estimated to be at risk of developing cancer.[19] In 1999, the cancer age-standardised (to the world population) incidence rates (ASR) were 148.9 and 134.9/100 000, in males and females, respectively. The five leading cancers in females, in order, were those of the breast, cervix, colorectum, oesophagus and corpus uteri. Cancers of the prostate, lung, oesophagus, colorectum and bladder were the five leading cancers in males.

White males had the highest ASR in 1999 (277.1/100 000) followed by coloured males (214.8), Asian (126.8) and African males (97.1). White females also had the highest ASR (230.5), followed by coloured (171.0), Asian (143.2) and African females (103.7). Because of serious under-reporting in the African population, age-standardised incidence rates are probably underestimated. It is interesting to note that while the age-standardised death rates for all cancers in males are higher than rates in females for each population group, NCR data shows that the overall cancer age-standardised incidence rates in African and Asian females are higher than those in males of the same population group.

Despite several limitations, the data compiled by the NCR are the only comprehensive source of information on the incidence of cancer in South Africa. As the NCR reflects national rates of histologically diagnosed cancer, these can form the basis of minimal estimation of incidence. Until now, these data have been used to inform development of the draft national policy guidelines for cancer prevention and control,[20] as well as to inform research and for teaching purposes.

### *2.4.2 The Umtata Registry*

The Umtata Registry[21] includes a large number of cases diagnosed among the residents of the Umtata district, the former Transkei 'homeland', in the Eastern Cape. Incidence rates were calculated for the period 1996 to 1998 using the census data for 1996. The overall cancer incidence is 141.3/100 000 in males and 105.8 in females. The most important cancers in males were cancers of the oesophagus (ASR 62.5), lung (ASR 15.7) and liver (ASR 16.0). In females, the main cancers were those of the oesophagus (ASR 34.5), cervix (ASR 26.3) and breast (ASR 14.9).[5]

### *2.4.3 The PROMEC rural districts' Registry*

A population-based cancer registry was established by the Programme on Mycotoxin and Experimental Carcinogenesis (PROMEC) of the Medical Research Council (MRC) in the Bizana, Butterworth, Kentani and Lusikisiki districts of the Transkei in 1981.[22] This population-based registry systematically and continuously registers all cancer cases identified within the defined geographical area. During the period 1996 to 2000, 1394 new cancer cases were reported by the PROMEC registry (552 males and 842 females).[23] The most common were oesophageal, cervical, breast, lung, prostate and liver cancers. The low overall age-standardised rates for all cancers (44.8/100 000 for males and 46.5 for females)[23] for the period 1996-2000 and some irregularity in numbers of cases registered by year and district suggest possible under-diagnosis and/or under-registration.[5] The reasons for the observed decrease in the number of cases in the four districts include, among others, a decline in health-care delivery services and poor record keeping leading to underreporting.[23] Despite these limitations, however, results from the PROMEC Registry should be treated as minimum levels of incidence of cancer in the four districts.[23]

### *2.4.4 Elim Hospital*

Data were collected at Elim Hospital in Limpopo Province during 1991-1994.[24] In males, the leading cancers were oesophagus (17.7%), mouth (16.5%) and liver (15.6%), while in females the main cancers were cervix (39.8%), breast (12.9%) and oesophagus (5%).[5]

Table 12.3. Summary incidence rates for the leading five cancers by population group and sex, South Africa 1998 and 1999[19]

| | 1998 | | | 1999 | | |
|---|---|---|---|---|---|---|
| Pop/Sex | Cancer | ASR | LR | Cancer | ASR | LR |
| Asian Female | Breast | 45.26 | 18 | Breast | 49.62 | 18 |
| | Cervix | 16.39 | 49 | Cervix | 11.02 | 81 |
| | Uterus | 11.76 | 65 | Colorectal | 7.31 | 99 |
| | Colorectal | 10.45 | 78 | Uterus | 7.13 | 106 |
| | Stomach | 6.5 | 120 | Ovary | 6.29 | 121 |
| | All | 164.59 | 6 | All | 143.24 | 7 |
| Asian Male | Prostate | 20.41 | 46 | Prostate | 18.34 | 39 |
| | Stomach | 12.8 | 64 | Colorectal | 14.28 | 51 |
| | Lung | 12.18 | 59 | Lung | 12.93 | 63 |
| | Colorectal | 11.01 | 94 | Stomach | 12.77 | 66 |
| | Leukaemia | 7.69 | 170 | Bladder | 10.46 | 108 |
| | All | 139.87 | 7 | All | 126.81 | 7 |
| Black Female | Cervix | 42.1 | 21 | Cervix | 34.88 | 25 |
| | Breast | 17.98 | 51 | Breast | 18.39 | 49 |
| | Oesophagus | 7.36 | 108 | Oesophagus | 6.95 | 113 |
| | Uterus | 3.92 | 193 | Uterus | 4.68 | 157 |
| | Ovary | 3.07 | 257 | Ovary | 2.76 | 313 |
| | All | 111.00 | 9 | All | 103.71 | 9 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Black Male | Prostate | 20.64 | 42 | Prostate | 17.17 | 50 |
| | Oesophagus | 15.59 | 53 | Oesophagus | 14.13 | 59 |
| | Lung | 12.07 | 68 | Lung | 9.28 | 87 |
| | Larynx | 4.37 | 193 | Larynx | 4.09 | 193 |
| | Stomach | 3.6 | 233 | Colorectal | 2.96 | 286 |
| | All | 109.94 | 9 | All | 97.11 | 10 |
| Coloured Female | Breast | 45.21 | 19 | Breast | 49.77 | 18 |
| | Cervix | 29.04 | 30 | Cervix | 26.35 | 34 |
| | Colorectal | 7.99 | 109 | Colorectal | 9.66 | 89 |
| | Lung | 7.55 | 100 | Lung | 9.65 | 76 |
| | Stomach | 6.8 | 118 | Uterus | 6.61 | 107 |
| | All | 158.98 | 6 | All | 171.04 | 6 |
| Coloured Male | Prostate | 47.14 | 17 | Prostate | 47.98 | 19 |
| | Lung | 20.15 | 38 | Lung | 23.48 | 32 |
| | Colorectal | 13.76 | 58 | Stomach | 16.25 | 51 |
| | Stomach | 13.55 | 63 | Colorectal | 14.09 | 56 |
| | Oesophagus | 13.36 | 59 | Bladder | 12.53 | 66 |
| | All | 202.59 | 5 | All | 214.79 | 4 |
| White Female | Breast | 76.04 | 12 | Breast | 76.46 | 12 |
| | Melanoma | 15 | 66 | Colorectal | 17.52 | 48 |
| | Colorectal | 14.99 | 58 | Melanoma | 16.73 | 61 |
| | Cervix | 14.5 | 67 | Cervix | 12.04 | 81 |
| | Ovary | 10.81 | 78 | Ovary | 10.07 | 82 |
| | All | 230.28 | 4 | All | 230.46 | 4 |
| White Male | Prostate | 78.51 | 10 | Prostate | 74.38 | 10 |
| | Colorectal | 23.74 | 35 | Colorectal | 25.44 | 31 |
| | Bladder | 23.74 | 35 | Bladder | 23.69 | 35 |
| | Lung | 21.7 | 35 | Melanoma | 20.94 | 43 |
| | Melanoma | 19.27 | 48 | Lung | 20.74 | 37 |
| | All | 284.55 | 3 | All | 277.13 | 4 |
| All Females | Cervix | 34.43 | 26 | Breast | 33.41 | 27 |
| | Breast | 32.70 | 27 | Cervix | 28.69 | 31 |
| | Colorectal | 5.83 | 154 | Colorectal | 6.61 | 131 |
| | Oesophagus | 5.95 | 136 | Oesophagus | 5.49 | 143 |
| | Ovary | 4.91 | 166 | Uterus | 5.09 | 146 |
| | All | 136.74 | 6 | All | 134.86 | 6 |
| All Males | Prostate | 37.59 | 22 | Prostate | 34.12 | 24 |
| | Lung | 15.18 | 52 | Lung | 13.56 | 59 |
| | Oesophagus | 12.56 | 65 | Oesophagus | 11.33 | 73 |
| | Colorectal | 9.44 | 92 | Colorectal | 9.74 | 83 |
| | Bladder | 8.63 | 98 | Bladder | 8.24 | 104 |
| | All | 156.18 | 4 | All | 148.87 | 5 |

ASR: Age-standardised incidence rate/100 000 (adjusted for unknown age); LR: Lifetime risk (0-74)

(All rates exclude BCC and SCC of skin)

## 2.5 CANCER BURDEN ATTRIBUTABLE TO SELECTED RISK AND LIFESTYLE FACTORS

Comparative Risk Assessment (CRA) of the SA NBD 2000 study was carried out using methodology developed by the World Health Organisation for its 2002 World Health Report.[25,26] The goal was to estimate the contributions of a selected group of major risk factors in various levels of causality to the burden of disease in 2000.[27] In line with the unique quadruple burden of disease in the country, preliminary results from the risk factor study show that the loss of health in South Africa is dominated, on the one hand, by risk factors related to poverty and underdevelopment, such as undernutrition, unsafe water, sanitation and hygiene and indoor smoke from solid fuels, and, on the other hand, by risk factors associated with a western lifestyle, such as alcohol and tobacco use, high blood pressure and high cholesterol levels. Unsafe sex is the leading risk accounting for approximately 31.5% of all healthy years of life lost in 2000.[27] Interpersonal violence is another important risk factor, which, together with alcohol, contributes to the high injury burden.

Population attributable fractions for the various risk and lifestyle factors that were analysed, where cancer is an adverse outcome of exposure, are presented in Table 12.4. These include mainly the diet-related risk factors, such as high body mass, low intake of fruit and vegetables, and physical inactivity, unsafe sex, the addictive substances tobacco and alcohol, as well as one of the environmental risks, exposure to indoor smoke from solid fuels. The prevalences of exposure to some of these risk factors are presented in Table 12.5.

Table 12.4. Population attributable fractions by risk factor and sex (% DALYs for each cause), South Africa, 2000 (adapted)[27]

| | Males | Females |
|---|---|---|
| **Other diet-related risks and physical inactivity** | | |
| High Body Mass | | |
| Post-menopausal breast cancer | - | 13 |
| Colorectal cancer | 12 | 22 |
| Endometrial cancer | - | 60 |
| Low fruit and vegetable intake | | |
| Oesophagus cancer | 24 | 24 |
| Stomach cancer | 24 | 24 |
| Colorectal cancer | 3 | 3 |
| Trachea/bronchi/lung cancers | 15 | 16 |
| Physical Inactivity | | |
| Female breast cancer | - | 17 |
| Colorectal cancer | 26 | 28 |
| **Sexual and reproductive health** | | |
| Unsafe sex | | |
| Cervix uteri cancer | - | 100 |
| **Addictive substances** | | |
| Tobacco | | |
| Mouth, oropharynx, larynx, oesophagus, sinus cancer | 58 | 25 |
| Trachea/bronchi/lung cancers | 78 | 62 |
| Digestive, urinary, cervical cancer | 16 | 3 |
| Other cancers | 14 | 4 |
| Alcohol | | |
| Mouth and oropharynx cancers | 29 | 16 |
| Oesophagus cancer | 37 | 23 |
| Liver cancer | 30 | 16 |
| Larynx cancer | 43 | 28 |
| Female breast cancer | - | 6 |
| **Environmental risks** | | |
| Indoor smoke from solid fuels | | |
| Trachea/bronchi/lung cancer | 2 | 4 |

Table 12.5. Summary prevalence of selected risk factors related to cancers by sex, South Africa 2000 (adapted)[27]

| | Prevalence criteria | Males | Females | Data source |
|---|---|---|---|---|
| **Other diet-related risks and physical inactivity** | | | | |
| High body mass | Mean body mass index (BMI kg/m$^2$) | 23.4 (SE 0.09) | 27.3 (SE 0.10) | SADHS 1998 adult data ages 15+ years[28] |
| | Proportion overweight (BMI 25-29.9) | 19.8% | 26.1% | |
| | Proportion obese (BMI 30+) | 9.3% | 30.1% | |
| Low fruit and vegetable intake | Average intake (g/day) | 219 | 219 | WHO/FAO 2003[29] |
| Physical inactivity | Proportion with no physical activity | 43.4% | 48.5% | WHS 2003[30] |
| **Addictive substances** | | | | |
| Tobacco* | Proportion currently smoke daily | 36.7% | 9.4% | SADHS 1998[28] adult data ages 15+ years |
| Alcohol | Proportion consuming alcohol | 44.6% | 16.9% | SADHS 1998 adult data ages 15+ years[28] |
| **Environmental risks** | | | | |
| Indoor smoke from solid fuels | Proportion households: | | | South African Census 2001[31] |
| | using solid fuels | 33% | 33% | |
| | using coal | 7% | 7% | |

* Current smoking prevalence not used in calculation of tobacco population attributable fraction, because of lag effect (method described by Groenewald *et al*. (unpublished data)

SE: standard error

WHS 2003: World Health Survey 2003

SADHS 1998: South African Demographic and Health Survey 1998

# 3 IMPORTANT LIFESTYLE-INDUCED CANCERS IN SOUTH AFRICA

## 3.1 Aerodigestive cancers

In the South African population, lifetime risks of developing cancer of the upper aerodigestive system (including oesophageal, lung, oral cavity, nasopharyngeal and laryngeal cancers) are 1 in 20 for African males and 1 in 76 for African females.[32] Tobacco and alcohol consumption appear to be important risk factors for their development. However, only a few studies from Africa have investigated the relative importance of these exposures.

## 3.2 Lung cancer

### *3.2.1 Descriptive epidemiology*

Lung cancer is the leading cancer worldwide, with an estimated 1.24 million new cases (12.3% of all cancers) having occurred in the year 2000.[1]

In South Africa in 2000, lung cancer, with its rather poor prognosis, was the leading cancer among males in terms of deaths (21.9% of all male cancer deaths)[15] but ranked second in terms of incidence (5.9% of all male cancers reported to the NCR in 1999).[19] In females, lung cancer ranked third in terms of deaths (10.9% of all female cancer deaths), and seventh in terms of incidence (2.4% of all female cancers). The age-standardised death rate for males was 42.3/100 000, with a much lower age-standardised incidence rate (ASR) 13.6/100 000. Lung cancer was more common from age 50 onwards, with an ASR of 28 in the 50-54-age group and peaking at ages 65-69 years, with an ASR of 89.

In females the age-standardised death rate was 13.8/100 000, and the ASR 4.4. Lifetime risk (age 0-74 years) of developing lung cancer was 1 in 59 in males and 1 in 177 for females in 1999.

The age-standardised mortality rate in 2000 was highest in coloured males and females (77.1 and 38.8/100 000, respectively), followed by white males and females (52.3 and 30.1, respectively). The death rate was lower in the African population at 31.1 and 6.3 for males and females, respectively, and lowest in the Asian population group (27.5 and 5.6 for males and females, respectively) (Table 12.2). The Western Cape had the highest lung cancer age standardized death rates, followed by the Eastern Cape and Gauteng provinces. Rates were lowest in Limpopo province (Fig. 9).

In 1999, the age-standardised incidence rate was also highest in coloured (23.5/100 000), and white (20.7) males, followed by Asian males (12.9), and lowest in African males (9.3), possibly because of underreporting in this population group. In females, age-standardised incidence rates in coloured and white females were similar and almost fivefold higher than in African females (9.7 vs. 2.0/100 000).[19] Coloured females, however, were at a slightly higher risk of developing lung cancer than white females (LR = 1 in 76 vs. 1 in 80, respectively).

Age-standardised rates reported for the Umtata Registry in the Eastern Cape were similar to the national incidence rates for the African population (15.7 and 3.6/100 000 for males and females, respectively) for the period 1996-1998, but lower incidence rates were reported in the PROMEC rural districts' registry for 1996-2000, (6.2 and 1.3 for males and females, respectively).[23]

The highest incidence rates for lung cancer occur in developed countries. Lung cancer rates in males in England (1993-1997, 53.1/100 000) were more than double the incidence rates in South African white and coloured males. In most developing countries, incidence rates are higher in the white population group than the black one, while in developed countries, such as the United States (1993-1997), the reverse is the case (ASR 86.5 for black vs. 55.6/100 000 for white people).[5] South African lung cancer incidence rates were higher than the West and Central African countries, such as Mali (4.8/100 000) and Uganda (1.5), but lower than North African countries, such as Tunisia. White male and female Zimbabweans in Harare (1990-1997) had the highest recorded lung cancer rates in Africa (ASR = 38.4 and 24.5, for males and females, respectively).[5] For African Zimbabweans (ASR for 1994-1997 = 12.1), rates were similar to South African rates in the African population in males, but for females, African females in Zimbabwe (5.9) experience double the incidence rate of African females in our country.

### *3.2.2 Lifestyle factors*

**Tobacco smoking**

Tobacco smoking is the leading cause of lung cancer,[33] with a clear dose-response effect related to both duration of smoking and amount smoked. In 1985, it was estimated that about 76% of all lung cancer worldwide (84% of cases in males and 46% in females) could be attributed to tobacco smoking.[34] Preliminary results from the South African CRA study indicate that 78% of the lung cancer burden in males and 62% in females could be attributed to tobacco in 2000 (Table 12.4). Indications of a role for smoking in the development of lung cancer among more urbanised African males from Johannesburg and KZN in South Africa, and Bulawayo in Zimbabwe, have been observed since the 1960s with the incidence of lung cancer already beginning to rise at that time.[35,36]

A more recent case-control study in Limpopo province described the first association between smoking and lung cancer in African females. Although tobacco smoking was shown to be the most important risk factor for the development of lung cancer, environmental exposure to asbestos, a 'dusty' occupation in males and indoor air pollution may also contribute to the development of lung cancer in this province.[37] In males, the risks associated with lung cancer were 9.4 in heavy smokers (1-14 g tobacco daily) and 12 in light smokers (15+ g daily), compared with non-smokers. Female current smokers had a 5.5-fold increased risk of lung cancer compared with non-smokers.[37]

In 1995, an ongoing case-control study was initiated among newly diagnosed African cancer patients admitted to Chris Hani-Baragwanath, Hillbrow and Johannesburg Hospitals, which are the main teaching and public referral hospitals for cancer patients in Johannesburg and Soweto in the Gauteng province. These data were analysed to estimate the importance of tobacco and alcohol consumption and other suspected risk factors with respect to cancer of the oesophagus (267 males and 138 females), lung (105 males and 41 females), oral cavity (87 males and 37 females) and larynx (51 males).[38] Cancers not associated with tobacco or alcohol consumption were used as controls (804 males and 13 70 females). In males the risks for lung cancer relative to non-smokers were 6.8 in ex-smokers, 6.2 in current light (1-14 g tobacco/day) smokers and 24.2 in current heavy (15+ g/day) smokers. Among females, the risks were 7.1 in ex-smokers, 10.7 in light smokers and 50.8 in heavy smokers.[38]

Estimates for smoking among South Africans vary considerably. In addition, usage varies between different communities, with smoking among coloured males and females being equally common, smoking by African females much lower than by African males, and the white community having intermediate rates.[39,40] In the South African Demographic and Health Survey (SADHS) of 1998, the national prevalence for current daily smoking was higher in African urban males (35.3%) than in white males (33.4%), although the prevalence in African urban females (5%) was lower than in white females (23.2%).[28]

The prevalence reported for the urban current daily smokers of all population groups in Gauteng was 35.5% for males and 10.8% for females.[28] The current cigarette smoking prevalence in the Johannesburg/Soweto case-control study was 32.8% for African males and 8.3% for African females in the control group.[38] A prevalence of 55% and 10% for males and females, respectively, was obtained for African adults in Gauteng from the multi-stage cluster sample survey conducted in 1995.[39] The lower rates found in the Johannesburg/Soweto case-control study could partially be explained by the fact that the study did not cover individuals who had access to private or company medical care.

Notwithstanding the limitations of cross-sectional studies, an analysis of adult data from the SADHS indicates that in the 25-34-year age group, the proportion of current daily smokers is about the same in African and white males. From age 35 years and older, the proportion of African men who are current daily smokers is actually higher than in whites (48.3% in African vs. 39.5% in white in the 35-44-year age group). It is only in the 15-24-year age group that African males have slightly lower smoking rates than white males.[40] African females, however, have much lower smoking rates than both white and coloured females at all ages.

Prevalence of cigarette smoking among South African grade 8-10 learners was 23%, with the highest rate reported among young coloured males (36%) and the lowest prevalence among African students (10.5%).[41] Although smoking rates are high in South Africa, average tobacco per capita consumption is lower than in countries with the highest lung cancer rates, particularly in the African population.[19]

The differences in smoking rates among the population groups at different stages of the health transition, as well as the gender differences, are reflected in the age-specific death rates for lung cancer presented in Fig. 6b. However, it is important to note that these death rates reflect exposure to tobacco in the past. Lung cancer death rates were highest in the coloured population in both genders, followed by white males and females. African males had lower rates than coloured and white males in the older age groups, but the lung cancer death rates in African males in the 35-44-year age groups (9 vs. 2/100 000) and 45-54 (57 vs. 30) are higher than in the white population (Fig. 6b).

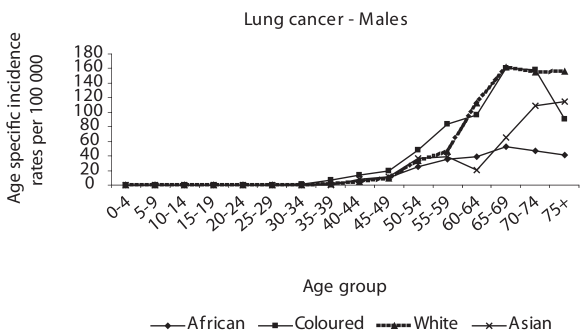


Figure 11: Age-specific incidence rates of lung cancer in males by population group, South Africa 1999[19]

Even with high levels of underreporting in the African population, the age-specific incidence rates for lung cancer in young African males were also higher than in young white males (6 vs. 4 in the 40-44-year, and 11 vs. 9 in the 45-49-year age groups). In the older age groups, the rates in African males were much lower than in white males (47 vs. 155 in the 70-74-year, and 44 vs. 155 in the 75+-year age groups) (Fig. 11). However, this was not observed in African females, where lung cancer incidence and death rates are lower at all ages.

The much lower smoking rates among female cases (45.4%), when compared to males (90.8%) in the Johannesburg/Soweto case-control study, indicates other causes for this cancer.[38] These could include among others, passive smoking (in the 1995 survey, 48% of all adults reported exposure to smoking by at least one household member),[39] exposure to indoor smoke from solid fuels during cooking and the presence of various infectious and inflammatory conditions, genetic, hormonal, and nutritional factors (males traditionally receive the best and most food when there are shortages).

**Nutrition**

In the comparative risk assessment study, preliminary results show that about 15-16% of all healthy years of life lost because of lung cancer could be attributed to low intake of fruit and vegetables (Table 12.4). The average daily fruit and vegetable intake per capita was very low (219 g in adults 15 years and older) in South Africa 2000 (Table 12.5).

**Indoor smoke from solid fuels**

Nationally, the proportion of households using solid fuels for cooking and heating is about 33%,[31] and it has been estimated that about 4% of lung cancer in females and 2% in males can be attributed to exposure to this risk factor (Table 12.4). In Limpopo province, about 80% of the population uses solid fuels as a primary source of energy for heating and cooking. Mzileni *et al*.[37] found a significant association between lung cancer and indoor pollution for both sexes combined (RR 2.0, 95% CI: 1.1-3.6) in this province. Contrary to what might be expected, the use of wood, coal or anthracite for heating was not a significant risk factor for lung cancer in the Johannesburg/Soweto case-control study. This may be attributable to low cumulative exposure since heating in the Johannesburg area is only necessary at night for a few months of the year, as winter days are mostly sunny and mild.[38]

### *3.2.3 Occupational exposure*

Because of its long involvement in asbestos mining and processing South Africa has one of the highest incidence rates of mesothelioma in the world.[5] Incidence rates in the white population are similar to those in other countries where asbestos was formerly mined, such as Australia.[5,42,43]

Lung cancer was associated with birth or residence in areas where asbestos was mined in the South African case-control study by Mzileni and colleagues.[37] The study by Parkin *et al*.[36] in Zimbabwe, however, found no association between lung cancer and occupation in asbestos mines. In Zimbabwe mainly chrysotile asbestos is mined, whereas in South Africa crocidolite and amosite (associated with a much higher risk of lung cancer), as well as chrysotile, are mined. Excess lung cancer risks related to asbestos exposure have been found in white miners (standardised mortality ratio (SMR) 1.4 for amosite and 2.0 for crocidolite).[44]

South African gold miners have been observed to be at an increased risk of lung cancer in various cohort studies.[45-47] Two case-control studies, however, did not show an association, with most of the excess risk in the miners caused by smoking.[48,49] In a study by Hnidzo *et al*.[50] in 1997, an increased risk of lung cancer was found in patients with prior silicosis, after adjustment for smoking, but not with uranium production. In the Zimbabwean study, Parkin *et al*.[36] also found an increased risk of lung cancer in subjects who reported having worked in mines extracting nickel and copper (after adjustment for smoking) but not gold, chrome or coal. In a study among South African iron moulders, a significantly increased proportional mortality ratio for lung cancer was found in those who died after the age of 65 years.[51]

A slight increase in lung cancer with an odds ratio (OR) of 2.9 (95% CI: 1.1-7.5) in males working in 'potentially noxious' industries was observed in the Johannesburg/Soweto case-control study.[38] This group of industries included: metal and non-metallic mineral, chemical, petroleum, coal, rubber, plastics, wood and paper manufacturing and processing; the motor vehicle industry; construction; and mining and quarrying.

## 3.3 Oesophageal cancer

### *3.3.1 Descriptive epidemiology*

The incidence of oesophageal cancer is high in the African populations of Eastern and Southern Africa and low in Northern, Western, and Central Africa. Despite certain data limitations making comparability difficult in some of the earlier surveys, South Africa has experienced an enormous increase in the incidence of this cancer since the 1950s.[10] The risk was much higher than the national average in the Eastern Cape Province, particularly the rural areas of the former Transkei 'homeland'[52,53] where nutritional factors and consumption of maize contaminated with Fusarium sp may play an important role. Since the mid-1980s, the incidence of this cancer has decreased, as shown in the declining proportion of oesophageal cancers over time reported to the National Cancer Registry. The reasons for these secular trends remain uncertain.

Data from the PROMEC Registry in the Transkei have also shown an apparent decrease in the incidence rate of oesophageal cancer. The overall incidence rates for oesophageal cancer during the period 1996-2000 were 31.2 and 21.8 (per 100 000) in males and females, respectively, whereas during 1991-1995 higher rates of 76.6 and 36.5 for males and females, respectively, were recorded. Oesophageal cancer remained the most common cancer reported in males and females during the period 1996-2000, accounting for 63% of all male and 44% of all female cancer cases.[23] Data for 1981-1984[54] and 1985-1990[53] suggest that the incidence of oesophageal cancer has been declining in the high-risk districts of Butterworth and Centane, and increasing in the low-risk districts of Bizana and Lusikisiki. In 1996-2000, the highest male age-standardised rates were still recorded in Centane (44.8/100 000), followed by Lusikisiki (35.0), Bizana (31.0) but with Butterworth, the more industrialised district with an urbanised community, having the lowest rates (14.2).[23] The reasons for this equalization of the oesophageal cancer rates are also unclear, but it is possible, given the high rates of migration and differences in access to health services and diagnostic facilities between the two regions, that some of the previous differences in risk may have been exaggerated.[5]

The national ASR (11.3/100 000 in males and 5.5 in females), as reported by the NCR for 1999, was two to three times lower than current rates in Centane, Bizana and Lusikisiki districts. NCR incidence data for 1999 indicates that oesophageal cancer ranked third in males (5.2% of all male cancers) and fourth in females (3%). The lifetime risk of developing oesophageal cancer in males dropped from 1 in 65 in 1998 to 1in 73 in 1999. The risk of developing cancer of the oesophagus in males was double that of females (1 in 143 in 1999).[19]

Marked population group differences exist with the highest incidence rates observed in the African population. Oesophageal cancer was the second leading cancer in African males (ASR 14.1) with a lifetime risk of 1 in 59 in 1999. Among African females (ASR 7.0), it was the third leading cancer and the lifetime risk of developing it was 1 in 113 in 1999.19 Survival from oesophageal cancer is poor and it ranks higher in terms of deaths. In South Africa, oesophageal cancer was the second leading cause of cancer deaths in males (16.7% of all cancer deaths) and the fourth leading cause of cancer deaths in females (9.9%). Mortality rates were highest in the African population group, followed by the coloured, white and Asian groups. Oesophageal cancer was the leading cause of male cancer deaths in the African population (age-standardised mortality rate 41.4) and the second leading cause of cancer deaths after cervical cancer in African females (17.6) (Table 12.2), with relatively young age groups affected and rates increasing steadily from age 35-44 years (Fig. 7). The poorer Eastern Cape Province had the highest age-standardised mortality rates for oesophageal cancer for males and females in the country (Fig. 9). Mortality rates were also high in the North-West province.

Incidence rates recorded for African males (17.2/100 000) and females (8.4) in Harare, Zimbabwe, 1994-1997, were slightly higher than national African rates reported by the NCR for 1999. The age-standardised incidence rate (62.5) recorded for males in Umtata (1996-1998) was the highest recorded in Africa.[5] This cancer also ranks high in countries such as Iran and China, and is a leading cause of cancer deaths among male African Americans. The aetiology is not clear as these countries have very different cultures and diets.[23]

### *3.3.2 Lifestyle factors*

**Tobacco and alcohol**

Worldwide, numerous case-control and cohort studies have shown that tobacco and alcohol increase the risk of oesophageal cancer, and that their joint effect is multiplicative.[33,55-57] Previous case-control studies from South Africa[35,58-60] and Zimbabwe[61] showed an elevated risk for tobacco smoking in the development of oesophageal cancer. Only a few local studies have shown that alcohol and tobacco consumption have independent (and combined) effects on risk.[10,38,62] The more recent studies will be discussed in detail.

A hospital-based case-control study in the former Transkei also found a positive association with smoking but not with drinking of traditional beer.[60] The 1988 hospital-based case-control study in Soweto, however, found that alcohol and tobacco had an independent and multiplicative effect on the risk of developing oesophageal cancer[10] with an OR of 39 observed in heavy drinkers who also smoked heavily.

In the more recent Johannesburg/Soweto case-control study, black males and females who smoked heavily (15+ g tobacco/day) had a six-fold elevated risk of developing oesophageal cancer compared with non-smokers. 'Frequent' alcohol consumption, on its own, caused a marginally elevated risk for oesophageal cancer (OR 1.7, 95% CI: 1.0, 2.9, for females and OR 1.8, 95% CI: 1.2, 2.8, for males). For alcohol consumption in combination with smoking, the risks for oesophageal cancer increased significantly (OR 4.7, 95% CI: 2.8, 7.9 in males, and OR 4.8, 95% CI: 3.2, 6.1 in females)[38] compared with lifelong non-smokers and non-drinkers. The reason for the discrepancies in these results may be that many earlier studies were conducted when the principal beverages had a low (2-4%) alcohol content.

**Nutrition**

Other risk factors for oesophageal cancer include poor socio-economic conditions,[63] poor nutritional intake, and a diet lacking in vitamins A and C, riboflavin, nicotinic acid, magnesium and zinc.[58,64] Contamination of maize with Fusarium verticillioides (previously known as Fusarium moniliforme) and the consequent ingestion of mycotoxins (possibly fumonisins) produced by this fungus may also play a role.[65,66] Many of the world's 'hot spots' for oesophageal cancer are in populations that are poor and consume restricted diets. Maize, which has low levels of niacin, riboflavin, vitamin C and other micronutrients, is the staple in the Eastern Cape. In addition, homegrown and stored maize is often contaminated with Fusarium species, which produce mycotoxins recognised as being 'possibly carcinogenic' by an IARC (International Agency for Research on Cancer) working group.[67] Contaminated ears are often used for brewing beer while the 'good' ears are consumed as porridge.

At an average intake per capita of only 219 g/day in adult South Africans, preliminary results from the Comparative Risk Assessment study indicate that about 24% of oesophageal cancer burden in South Africa in 2000 could be attributable to low intake of fruit and vegetables.

**Residence in the Eastern Cape**

Various studies have been conducted in the former Transkei region of the Eastern Cape, where high incidences of oesophageal cancer were first recorded in 1955-1969.[52] The Johannesburg/Soweto case-control data confirm a higher risk for oesophageal cancer, following adjustment for other factors, for those patients who had lived in that area. Contrary to studies conducted in the Transkei, the case-control study found greater risks for females (OR 14.7, 95% CI: 4.7, 46.0) than for males (OR 3.1, 95% CI: 0.9, 10.8) of developing oesophageal cancer with 35 or more years of residence in the Eastern Cape. This can be explained by the fact that the Transkeian studies looked at individuals who were probably full-time residents of that area, whereas in the case-control study the males may have been migrant workers who still considered Transkei their home but who worked in the Johannesburg area most of the time.[38]

### 3.3.3 *Infections*

Infection with human papilloma virus (HPV) type 16 has been implicated as a risk factor for oesophageal squamous cell carcinoma, although the evidence is inconsistent.[68,69] It is possible that HPV is just an indirect measure of poorer environmental conditions known to be risk factors for the development of oesophageal cancer.

### 3.3.4 *Genetic factors*

Increased risks of oesophageal and upper-digestive tract cancers have been found in relation to the presence of the mutant allele of aldehyde dehydrogenase 2 (ALDH*2) in Japan.[70] ALDH2 is a key enzyme that eliminates acetaldehyde formed from alcohol. The mutation in ALDH*2 leads to inactivity of the enzyme and accumulation of acetaldehyde, which is thought to be a carcinogen. The relevance of ALDH2 metabolism in the epidemiology of oesophageal cancer in Africa, however, is unclear.[5]

## 3.4 Oral cancer

Oral cancers include cancers of the lip (excluding skin of lip), tongue, gum, mouth and salivary glands. Cancer of the mouth is the most common oral cancer in South Africa. It is more prevalent in males, comprising 1.5% of all male cancers but only 0.6% of all female cancers.

The risk of developing mouth cancer in males was more than three times that in females (1 in 254 for males, and 1 in 861 for females in 1999). The age-standardised incidence rate for cancer of the mouth was the highest in African males (2.8/100 000 in 1999) being the eighth leading cancer in this group. Age-standardised rates were also high for Asian females (2.8) and lowest in African females (0.7).[19] Incidence rates for cancer of the mouth are highest in Bombay, India. Female South African Asians rank second (to Indian females) worldwide and African males rank third in the world, with only males in India and blacks in the United States reporting higher rates.[19]

Mouth and oropharynx cancer ranked eleventh in South Africa in terms of deaths accounting for 3.3% of all cancer deaths in 2000. Age-standardised death rates were highest in coloured males (17.3), followed by African males (7.7) and then white males (6.7). Although Asian males had the lowest death rates, Asian females had the highest age-standardised mortality rates (5.2) among females in South Africa, 2000 (Table 12.2).

### *3.4.1 Lifestyle factors*

**Tobacco and alcohol**

Tobacco is a risk factor for oral cancers, whether smoked[33] or chewed.[71] Chewing the areca (betel) nut is an important risk factor in Asian communities worldwide, including South Africa. Alcohol consumption is another important risk factor[55] and acts multiplicatively with smoking.[5] Differences in the prevalence and use of tobacco and alcohol may explain the differences in incidence between males and females in the different population groups.

In the Johannesburg/Soweto case-control study the OR associated with light smoking (1-14 g tobacco/day) in males was 6.1 (95% CI: 2.5, 14.8) and with heavy smoking (15+ g/day) it was 12.5 (95% CI: 4.6, 33.5). In females, the OR associated with light smoking was 3.9 (95% CI: 1.5, 10.3) but the risk of developing oral cancer was not significantly increased in female heavy smokers, possibly because of small numbers (OR 6.2, 95% CI: 0.9, 44.2). Daily alcohol consumption, adjusted for smoking, did not significantly increase the risk of developing this cancer in either sex.[38] Several studies have shown a significantly increased risk of developing mouth and oropharynx cancers with increased alcohol consumption, and preliminary results from the South African CRA study show that about 29% of the burden from mouth and oropharynx cancer in males and 16% in females is attributable to alcohol consumption (Table 12.4).

**Nutritional factors**

Diets low in fruit and vegetables, possibly because of a low intake of micronutrients, especially vitamin C, have been found to increase the risk of developing this cancer.

**Infections**

The HPV appears to play an aetiological role in cancers of the oropharynx and possibly oral cavity.[72] HPV-16 was the most common type of HPV DNA detected in tumour tissue.[72]

## 3.5 Laryngeal cancer

Laryngeal cancer was the eighth leading cancer in males (2.1% of all male cancers) with an ASR of 4.7/100 000 in 1999. The lifetime risk of developing cancer of the larynx in males was 1 in 168 in 1999. Cancer of the larynx was less common in females, comprising only 0.4% of all female cancers per year (ASR 0.8 in 1999).

Although laryngeal cancer was the fourth leading cancer in African males and ranked lower in the other population groups, coloured males had the highest incidence rate of laryngeal cancer (10.0), followed by white (5.2), African (4.1) and Asian males (1.1). In terms of age-standardised mortality rates, Asian males had the highest rates (11.5), followed by coloured (10.2), African (4.9) and white (4.1) males. Females of all population groups had very low and similar mortality rates.

### *3.5.1 Lifestyle factors*

**Tobacco and alcohol**

In the Johannesburg/Soweto case-control study, 51 male cases of laryngeal cancer were compared with 804 controls with cancers not associated with tobacco or alcohol. Females were not included in the analysis because of the small number of cases. Almost all the males (49/51) with laryngeal cancer smoked. The risk of developing the cancer was significantly increased in both light (1-14 g tobacco/day) (OR 10.2, 95% CI: 2.1, 49.3) and heavy

(15+ g/day) (OR 23.6, 95% CI: 4.6, 121.2) smokers compared with non-smokers. Although a strong body of evidence exists for an increased risk of this cancer with increased alcohol consumption, this was not observed in the case-control study.[38] Results from the South African CRA study show that about 43% of laryngeal cancer burden in males is attributable to alcohol consumption (Table 12.4).

## 3.6 Female breast cancer

### *3.6.1 Descriptive epidemiology*

Breast is the most common cancer in females worldwide and accounts for about one quarter of all female cancers.[73] The WHO estimates that just over a million new breast cancer cases occur worldwide annually. Increasing breast cancer trends are reported particularly in previously low incidence regions, including Africa and Asia, and increases greater than 1% per year have been reported in developing countries.[5,74,75] In Uganda, increasing breast cancer incidence rates have been observed since 1960.[76]

Breast cancer was the second leading cause (15.6%) of cancer deaths in females in South Africa in 2000 (Table 12.1). The more developed provinces, Western Cape and Gauteng, had the highest age-standardised breast cancer deaths rates, with Mpumalanga having the lowest rate (Figs. 8 and 9).

Breast cancer was the leading cause of cancer deaths among South African white females. The age-standardised death rate was highest in white females (35.2/100 000), almost three fold higher than in African females (12.7), followed by coloured (32.7) and Asian females (28.5). The age-specific death rates for breast cancer by population group are shown in Fig. 7. Death rates are very similar in the younger age groups (2 in African, 1 in coloured and 4 in white females in the 25-34-year age group, and then 10 in African, 18 in coloured and 17 in white females in the 35-44-year age group). It is only in the older age groups that African females have much lower rates (101 in African females compared with 295 in white females in the 75+-year age group). This pattern is also evident in terms of incidence.

Breast cancer was the leading female cancer in terms of incidence in 1999. In that year, 19.4% of all the cancers reported to the National Cancer Registry were breast cancer (5589 cases). The age-standardised incidence rate in 1999 was 34.6/100 000 and the risk of developing breast cancer in females was 1 in 26 in the age range 0-74 years (Table 12.3).[19] About 50% of female breast cancers occur in women 55 years and older. Breast cancer incidence rates increase with age with rates as high as 162/100 000 in the 75+-age group. Much lower rates were reported in women younger than 55 years: the age-specific incidence rate in women aged 35-39 years was about 24. Similar rates were reported in a study in the Western Cape on African and coloured females younger than 55 years, which showed an overall incidence rate of 23 in 1994/5.[77] About 58% of the breast cancers in women younger than 55 years were diagnosed at stages 1 and 2, while 42% were diagnosed at advanced stages (3 and 4).[77]

There are also marked differences in incidence among the different population groups. Since the establishment of the NCR in 1986, breast cancer has been the leading incident cancer in white females, with ASRs ranging between 64 in 1993 to 76.5 in 1999, and a lifetime risk as high as 1 in 12 in 1999.[19,32] Coloured and Asian females had similar ASRs of 49.8 and 49.6, respectively,[19] with a lifetime risk of developing breast cancer of 1 in 18. In 1999, the national overall incidence rate in African females was 18.4. Again, the differences in rates between the white and African females are more pronounced in the older age groups, while in the younger age groups, the incidence rate in African females is closer to that of white and coloured females (Fig. 12).

Incidence rates for breast cancer appear to have been increasing in the four districts of the Transkei region from 1996-2000 when compared with the 1985-1990 and 1991-1995 periods.[23] Breast cancer was the third most common cancer among women reported to the PROMEC cancer registry from 1996-2000, accounting for 16% of all female cancers. Incidence rates in African women in the more urban Butterworth district (14.9) were similar to national rates for African women, with much lower rates reported in the Centane (6.1), Bizana (5.6) and Lusikisiki (3.7) districts.[23]

Breast cancer rates in sub-Saharan Africa are significantly lower than those reported for other continents. In Africa, white women in Harare, Zimbabwe, had the highest rates (ASR for 1990-1997 121.2), followed by South African white women (ASR for 1999 76.5). Despite the underreporting of the NCR in South Africa, rates in African females are comparable with those reported in developing countries. However, rates in South African Asian females are almost double those reported in Bombay, India.[19]

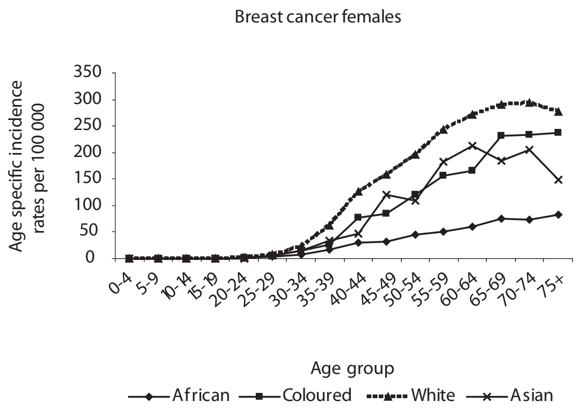


Figure 12: Age-specific incidence rates for female breast cancer by population group, South Africa 1999[19]

### *3.6.2 Reproductive factors*

Reproductive and hormonal factors are the most important known risk factors for breast cancer.[5,73,74] Breast cancer is known to occur more frequently among women with the following history: early menarche; who are either nulliparous, have few children or have their first birth at late age; and have a late menopause. Young coloured females who began menstruation at age 13 were found to have slightly increased, but not statistically significant, risk of developing breast cancer (OR 1.3, 95% CI: 0.8, 2.0) relative to those starting at age 17 or older ages. Although this association appeared stronger among African females (OR 1.9, 95% CI: 0.5, 7.4), it was also not statistically significant.[78] Deliveries occurring before age 30 have been shown to have a protective effect,[79] while in Uganda Ssali *et al*.[80] showed an increased breast cancer risk from age of delivery of 22 years or more (OR 4.3, 95% CI: 1.7, 10.8).

Available evidence shows no association between the use of injectable progestogen contraceptives and the development of breast cancer.[81,82] A small but increased risk (OR 1.2, 95% CI: 1.0, 1.5) was found in African and coloured females who were using oral contraceptives and this association was strongest in females younger than age 35 (OR 1.7, 95% CI: 1.0, 3.0).[81] Post-menopausal oestrogen therapy showed a small increase in risk with longer duration of use, while hormone replacement therapy (HRT) in post-menopausal females has shown a two-fold increased risk in current users, compared to never-users.[83]

### *3.6.3 Lifestyle factors*

The risk of breast cancer is clearly associated with socio-economic status, with females with higher education or income being at higher risk.[5,84] These differences may be attributable to the prevalence of risk factors between the social classes, such as the reproductive factors mentioned above and other known risk factors for the disease including alcohol consumption, diet, smoking, body weight, physical activity and genetic factors. The evidence of smoking on breast cancer remains inconclusive. Increased body weight has been found to increase the risk, whereas physical activity has been found to be beneficial at all ages in reducing risk. Physical inactivity, though, has harmful effects and the prevalence of this risk factor is extremely high in South Africa. As a result, preliminary results from the risk factor study indicate that about 17% of breast cancer cases are attributable to physical inactivity. Obesity is another common problem, and high body mass accounts for about 15% of post-menopausal breast cancer. Hazardous and harmful alcohol consumption is low among females in South Africa and hence only about 6% of breast cancer can be attributed to this risk factor.[27]

### *3.6.4 Genetic factors*

Familial risk of breast cancer is mediated through the major susceptibility genes BRCA1 and BRCA2. Around 2% of breast cancers are likely to be attributable to BRCA1 mutations in European females. Not much is known of the prevalence of mutations in BRCA1 and BRCA2 in African populations.[5]

## 3.7 Liver cancer

The highest liver cancer incidence rates have been reported in Western and Central Africa, Eastern and South Eastern Asia and Melanesia. In most countries, males were at least twice as likely to develop liver cancer as females.

Low incidence rates were observed in South Africa. Liver cancer is grossly under-reported by the NCR because the liver is not commonly biopsied. This is largely because of complications, as well as the widespread availability of less invasive methods of diagnosis, such as alpha-fetoprotein (AFP) and sonography. Unfortunately, the NCR does not receive reports on AFP levels from pathology laboratories.

Liver cancer only comprised about 1.2% of all male cancers reported to the NCR in 1999. The lifetime risk of developing liver cancer in males was almost twice that in females (1 in 369 in males and 1 in 695 in females). The age-standardised incidence rate was highest in African males (2.6/100 000) and females (1.3).

As this cancer has a very poor prognosis, the number of deaths should not be very different from the number of new cases. Underreporting of liver cancer to the NCR resulted in age-standardised death rates being much higher than age-standardised incidence rates in South Africa. Liver cancer was the fourth leading cause of cancer death in males (7.8% of cancer deaths) and the sixth in females (4.9% of cancer deaths). The age-standardised mortality rate was highest in the African population (16.3 and 6.6, for males and females, respectively). The coloured population ranked second (9.1 and 8.6), followed by Asians (7.7 and 6.5) and whites (7.8 and 5.1).

Low incidence rates were also reported for African males by the PROMEC Registry. The highest incidence rates were reported in Centane and Bizana (both had ASRs of 4.1), followed by Lusikisiki (3.8) and Butterworth (3.2), with very low rates reported for females in all districts.[23] Other countries in Africa had much higher incidence rates of liver cancer; for example, The Gambia (ASR 48.9 in males for 1997-1998) and Africans in Harare in Zimbabwe (ASR 26.0 in males for 1994-1997).

### 3.7.1 Infections

**Hepatitis B infection**

Many case-control studies have confirmed the relationship between infection with hepatitis B virus (HBV) and liver cancer.[85] The recognition of the hepatitis C virus (HCV) and its role in hepatocarcinogenesis is more recent.[85] It seems that HCV causes liver cancer by chronic hepatitis and cirrhosis, both known to act as precursors of liver cancer through the intense hepatocyte regeneration occurring in these conditions.[5]

In a South African case-control study of the relative roles of hepatitis B and C in the aetiology of hepatocellular carcinoma in black hospital patients, the presence vs. absence of HBV surface antigen (HBsAg) (OR 21.8, 95% CI: 8.9, 53.4), as well as the seroprevalence of antibodies to HCV (HCV Ab) (OR 6.1, 95% CI: 2.8, 13.7) were associated with a significantly increased risk of hepatocellular carcinoma.[86] The effects of combined infection with HBV and HCV are not very clear. Kew *et al*.[86] observed an 82.5-fold increased odds of developing liver cancer in patients who were both HBsAg and HCV Ab seropositive.

### 3.7.2 Lifestyle factors

**Aflatoxin contamination of local food samples**

Aflatoxins are produced by moulds of the *Aspergillus* species, which infect stored grains and nuts. Aflatoxin B has been classified by IARC as a human carcinogen. In Africa, high levels of contamination have been found, particularly in groundnuts and maize. Significant rank order correlations between aflatoxin intake and primary liver cancer incidence in gold miners in the former Transkei districts were observed.[87]

**Alcohol consumption**

Alcohol consumption is another important risk factor. English *et al*.[88] found a 45% elevated risk of liver cancer in males and females who drink responsibly, while the risk was increased three-fold in males and 3.6-fold in females who drank in the hazardous and harmful alcohol categories. Results from the South African CRA study indicate that 30% of liver cancer burden in males and 17% in females are attributable to alcohol consumption (Table 12.4).

## 3.8 Non-melanoma skin cancers

Non-melanoma skin cancers are often difficult to ascertain because these cancers, although very common, are rarely fatal. Completeness of registration varies widely. About 2.75 million new cases of skin cancer are diagnosed worldwide every year.[89] Around 75% of skin cancers are of basal-cell origin (BCC), about 22% are squamous-cell (SCC), and about 3% are other skin carcinoma.[90] In Africa, incidence rates are low in the black and high in the white population.

In 1999, about 23% and 16% of all new cancers in males and females, respectively, were BCC, and about 7% and 4% in males and females, respectively, were SCC. Combined, these non-melanoma skin cancers comprised relatively high proportions of all male and females cancers every year. As opposed to melanoma, which develops later in life, non-melanoma skin cancers occur at younger ages. In males in 1999, age-specific incidence rates in the 35-39-year age group were as high as 20/100 000, increasing to 884 at ages 75 and older. The estimated risk in males in 1999 was about double that of females: 1 in 12 South African males and 1 in 25 females had a lifetime risk of developing this cancer, with an ASR of 74.5 for males and 38.6 for females.[19]

More than 80% of non-melanoma skin cancer reported to the NCR during the period 1998/99 occurred in the white population (both sexes). The highest ASR occurred in white males and females (271.1 and 149.9, respectively). The lifetime risk of developing this cancer was 1 in 4 in white males and 1 in 7 in white females. ASRs were also high in the coloured population group (62.9 and 30.8 in males and females, respectively). Age-standardised incidence rates were low in Asian and African population groups.

Whites in Zimbabwe had the highest incidence rates in Africa (635.3) for the period 1990-1997.[5] Both melanoma and non-melanoma skin cancer incidence rates in white South Africans were high and similar to that observed in Australian Caucasians but about four-fold higher than rates reported in the UK and France.[5,19] The African population in South Africa had higher incidence rates than seen in other parts of Africa, probably because of the fairer skin in black South Africans compared with a darker skin in other parts of Africa.

Non-melanoma skin cancer ranked very low in terms of deaths, accounting for only 0.6% of all cancer deaths in South Africa 2000. Age-standardised deaths rates were low in all population groups.

### *3.8.1 Lifestyle factors*

Susceptibility to skin cancer is inversely related to the degree of melanin pigmentation. The incidence of non-melanoma skin cancer increases in frequency with increasing proximity to the equator and fair-skinned populations exposed to ultra violet (UV) radiation are at high risk.

In Africa, these cancers also commonly occur because of depigmentation attributable to chronic scarring, and have been associated with tropical scars.[5,19] The majority of these are SCC and usually located in the lower limbs. SCC following leg ulcers was shown to decrease in Tanzania because of improved treatment of tropical ulcers and better nutrition.[5]

## 3.9 Prostate cancer

On a global basis, prostate cancer is the third most common cancer in males with most of this cancer burden occurring in Europe and North America. A general increase in prostate cancer rates has been reported worldwide.[5,91]

Increases in prostate cancer incidence rates are mainly attributable to the increasing use of the prostate specific antigen (PSA) diagnostic test as a screening tool. Between 1988 and 1994, the incidence rate of prostate cancer in New South Wales, Australia, rose by 125%, and overall the age-standardised mortality rate fell by 19% between 1991 and 2001.[92] Prostate cancer incidence rates are therefore largely influenced by screening. Incidence rates are likely to increase in population groups where screening for this cancer is common.

In South Africa, the incidence rate in white males has increased almost three-fold, but this increase was not observed in African males. The ASR in white males increased from 27.1 in 1988, to 63.5 in 1997, to 74.4/100 00 in 1999[19,93,94] The increase in ASR for African males has been relatively small: from 14.4 in 1988 to 17.2 in 1999. Further studies are needed to confirm the accuracy of prostate cancer incidence rates in the African population in South Africa, to help resolve the uncertainty around underreporting in this group.[19]

Prostate cancer was the leading incident cancer in males in 1998 and 1999, comprising, on average, 13-14% of all male cancer cases. The age-standardised incidence rate was 34.1 for males in 1999 with a lifetime risk of developing the disease of 1 in 24.[19]

A shift from oesophageal cancer as the leading incident cancer in African males to prostate cancer from 1996 onwards was observed by the NCR. Prostate cancer is now the leading male cancer in all population groups. The risk of developing the cancer in whites in 1999 (1 in 10) was twice that in coloureds (1 in 19), four times that in Asians (1 in 39) and five times that in Africans (1 in 50).

This is a cancer of the elderly, with more than 75% of cancers worldwide occurring in males aged 65 years and older and the risk increasing steeply with age. This steep increase was observed in both age-specific incidence and death rates in South Africa (see Fig. 3 for death rates).

In terms of deaths, prostate cancer is the third leading cancer in men, accounting for 11.8% of all male cancer deaths. The age-standardised mortality rate for all males in South Africa in 2000 was 26.8/100 000. White males had the highest age-standardised deaths rates (41.1), followed by coloureds (33.2), Africans (22.9) and Asians (13.2). In white men, the ratio of incidence to mortality for this cancer is 1.8, while in Africans the death rate is actually higher than the incidence rate.

The overall incidence of prostate cancer in the four districts of the Transkei was low (3.6) compared with national rates reported by the NCR. The more industrialised district of Butterworth had the highest ASR (7.4), followed by Centane (3.5), Bizana (2.1) and Lusikisiki (1.3).

Relatively high incidence and mortality for this cancer have been recorded in African populations and in populations of African descent.[5] In the United States, the incidence rate in the black population is about 72% higher than the white population.[5] The higher rates in the South African white population probably reflect better access to modern diagnostic and treatment methods, as well as testing for PSA.

### *3.9.1 Lifestyle factors*

The environmental risk factors for prostate cancer are not well understood. Several studies have implicated dietary fat in the aetiology of prostate cancer, and there is a strong association with intake of animal products, especially red meat. There is little evidence of a link with high body mass or for a protective effect from high fruit and vegetable intake and physical activity.

### *3.9.2 Genetic factors*

Genetic factors rather than diet may explain observed racial differences and elevated risk in men with a family history of prostate cancer, but no studies have been carried out in Africa.

### *3.9.3 Infections*

In a recent study by Fernandez *et al*. 2005,[95] the risk of prostate cancer increased among males with a history of sexually transmitted infections (OR 1.7, 95% CI: 1.1, 2.5) and among males who reported having sexual intercourse more than 7 times per week compared with males who reported a weekly frequency of 3 times or less (OR 2.1, 95% CI: 1.2, 3.7). This study supports the hypothesis that an infectious factor related to sexual behaviour could be involved in the occurrence of the cancer.

## 3.10 Colorectal cancer

Colorectal cancer is the second most common fatal malignancy in affluent societies (second to lung cancer) but rarer in developing countries. In 2000, colorectal cancer was the fourth most common cancer in the world. About 945 000 new colorectal cases are reported worldwide each year.[5,96] A general increase in international incidence trends for cancers of the colon and rectum was reported during 1960-1980 in both sexes.[97,98] Data from Uganda showed an increase in colorectal cancer incidence rates of more than two-fold from 1960-1966 to 1995-1997 (ASR of 3.0/100 000 to 6.8 in males, and from 2.7 to 6.6 in females).[76]

Earlier data from the 1960s showed that a large proportion of colon cancers in Africa occurred mostly on the left side.[5] Recent studies conducted at Pelonomi Hospital in South Africa, Ghana and Nigeria show that most colorectal cancer patients presented late with advanced disease and a higher proportion on the right side.[99-101]

In South Africa, colorectal cancer is the sixth leading cause of cancer deaths among males (5.4%) and the fifth among females (6.9%). Colorectal cancer is an important cause of cancer deaths in the white population. The age-standardised death rate was more than 5 times greater in the white population (22.6) compared with the African population (4.3).

In 1998/1999, colorectal cancer comprised 3.7% of male and 3.4% of female cancer incident cases and ranked fourth and third in males and females, respectively.[19] The age-standardised incidence rate for colorectal cancer in males was 9.7, while that in females was lower 6.6. Colorectal cancer incidence rates were also highest among white males and females (Table 12.3).

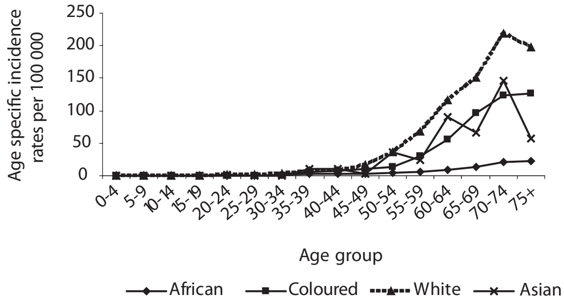


Figure 13: Age-specific incidence rates for colorectal cancer in males, South Africa 1999

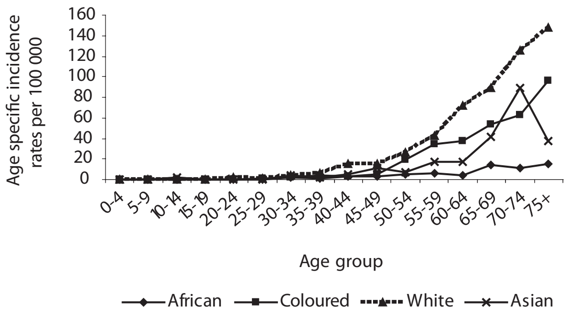


Figure 14: Age-specific incidence rates for colorectal cancer in females, South Africa 1999[19]

In 1999, colorectal cancer was the second leading cancer in white males and females. Asian and coloured males had similar ASRs with the lowest rates reported in African males.[19] The incidence rates in the white population (ASR 25.4/100 000 in males and 17.5 in females) were more than eight times the rates found in African males (3.0) and females (2.3).

Colorectal cancer incidence increases with age. Before age 40 years, the risk is higher among individuals with genetic predisposition or predisposing conditions, such as chronic inflammatory bowel disease.[102] In a 15-year study conducted at Groote Schuur Hospital, 47 colorectal cancer patients younger than 30 years were reported, with a higher incidence among the coloured population.[103]

Age-specific incidence rates for colorectal cancer by population group are illustrated in Figs. 13 and 14. An increasing risk in younger Africans may be the result of changing lifestyle and diet, resulting in a narrowing of the incidence gap observed in elderly South Africans. At young ages the incidence and death rates of the African, white and coloured population groups are almost the same (Fig. 6a, Figs. 13 and 14). At older ages there is a nine-fold difference in incidence in the older groups (in males 75 years and older: ASR 198 in white, 127 in coloured, 57 in Asian and 22 in Africans). However, there is very little difference in incidence in the younger age groups (in males 40-44 years: ASR 8 in coloured and white males, and 3 in Africans). This was also observed in terms of age-specific death rates (Fig. 6a).

Colorectal cancer rates in Asian, coloured and white South Africans are intermediate between those reported in developed and developing countries. NCR rates in Africans were two- to three-fold lower than those reported in other African countries, such as Africans in Zimbabwe (7.4 in males and 6.7 in females in 1994-1997). However, rates in Asian South Africans were 2.5 times higher than in Bombay, India, probably reflecting different diets and lifestyles led by these groups.

### 3.10.1 *Lifestyle factors*

**Diet-related risk factors and physical inactivity**

The risk of developing colorectal cancer is determined by local environmental conditions within the bowel.[104] Diets high in calories, rich in animal fat and poor in vegetables and fibre are associated with increased risk while physical activity is known to be protective.[105,106] About 10% of colorectal cancer burden in males and 20% in females in South Africa can be attributed to high body mass, 3% to low fruit and vegetable intake, while higher proportions, 26% and 28% of colorectal cancer burden in males and females, respectively, can be attributed to physical inactivity (Table 12.4). The joint effects of these risk factors on colorectal cancer have yet to be determined.[27]

**Tobacco and alcohol**

Some case-control studies investigating the effect of smoking on colorectal cancer have shown a positive association in males, with ORs ranging between 1.5 (95% CI: 1.1, 2.1) and 1.7 (95% CI: 1.3, 2.3) for smokers smoking more than 20 pack-years and rectal cancer. Among non-smokers exposed to cigarette smoke, a 50% increased risk was observed (OR 1.5, 95% CI: 1.1, 2.0).[107] However, other studies have shown no effect and colorectal cancer does not appear to be associated with smoking. Evidence for a causal relationship between alcohol and colorectal cancers has not yet produced consistent results.

**Other risks**

Ulcerative colitis, Crohn's disease, and therapeutic pelvic irradiation are other known risk factors for colorectal cancer. Crohn's disease increases the risk of colorectal cancer three-fold.[108] Studies on the association of nitrate (in public water supplies) with colorectal cancer show an increased risk for nitrate exposure levels averaging more than 5 mg/L over a period of 10 years among susceptible populations, such as subpopulations with low vitamin C intake (OR 2.0, 95% CI: 1.2, 3.3) and high meat intake (OR 2.2, 95% CI: 1.4, 3.6).[109] Other risk factors that were significantly associated with high risk of colon cancer include intestinal bacteria *Bacteroides vulgatus, Bacteroides stercoris, Bifidobacterium longum* and *Bifidobacterium angulatum*. Lactobacillus SO6 and *Eubacterium aerofaciens* are associated with low risk while total lactobacilli were found to be inversely related to risk.[5,110] Certain inherited conditions like hereditary polyposis coli are known to predispose persons to large bowel cancer, but the frequency of these conditions in the South African population is unknown.

## 3.11 Bladder cancer

Bladder cancer is the ninth most common cancer worldwide and accounts for two-thirds of all urinary tract cancers. About 336 000 new bladder cancer cases are reported worldwide every year.[96]

In South Africa, bladder cancer occurs most frequently in males with a risk three-fold higher than in females. In 1999, bladder cancer was the fifth most common cancer in males (3.5% of all cancer cases) with an ASR of 8.2/100 000. In females, it ranked eleventh with an ASR of 2.4.

In 1999, bladder cancer was the third leading cancer in white males with the highest ASR of 23.7 and a lifetime risk (0-74 years) of 1 in 35. In both coloured and Asian males, bladder cancer ranked fifth in 1999. In 1999, the incidence rate in African males (ASR of 1.5 and a lifetime risk of 1 in 527) was about 16 times lower than that observed in white males. The pattern in females was similar to that in males. White females had the highest incidence rates (6.3), followed by coloured (2.8) and Asian (1.8) females with African females having the lowest rates (0.8).[19]

The prognosis is good for this cancer and hence bladder cancer ranks much lower in terms of deaths. Bladder cancer was the 12$^{th}$ leading cause (2.2%) of cancer deaths in males and the 16th leading cause (1.0%) of cancer deaths in females. Age-standardised mortality rates were about four-fold higher in males (4.7) than in females (1.2). The highest age-standardised death rates were observed in coloured males (9.6), followed by white males (8.7), Asian males (4.0) and lowest in African males (2.4). Death rates were very low in African and Asian females.

Bladder cancer is characterised by marked differences in histology between African and white South Africans. In Africans, 36% of bladder cancers are squamous cell carcinomas (SCC) and 41% transitional cell carcinomas (TCC). Among whites, 2% are SCC and 94% are TCC.[5]

African males compare well with males from other African countries with low rates of 1.9 in 1997[94] and 1.5 in 1999[19] compared with Uganda (2.9 in 1993-1997) and Setiff in Algeria (4.0 in 1993-1997). Incidence rates in Africans in Harare (7.1 in males and 8.5 in females in 1994-1997) are several-fold higher than those in Africans in South Africa and most other African countries, with similar incidence in males and females. Incidence rates in South African Asians are high and are four times those reported in Bombay, India. Incidence trends for this cancer appear to be increasing moderately or steadily in many parts of the world, including Europe, Asia, and America, except for Columbia where an average decrease of 35% was reported in both sexes.[98]

### *3.11.1 Lifestyle factors*

**Tobacco**

Cigarette smoking is the most important risk factor for bladder cancer and shows a linear increasing relationship with the number of cigarettes smoked per day and the duration of smoking. In developed countries, 65% of all bladder cancer cases in males and 30% in females are attributable to tobacco.[5,96] Provisional results from the South African CRA study indicate that about 18% of bladder cancer in males can be attributed to tobacco.[27]

Epidemiological studies (that controlled for confounders) showed that the risk of bladder cancer is significantly increased in male smokers (OR 6.6, 95% CI: 3.1, 13.9). The strength of the association depends on the histological type, with the risk higher for TCC (OR 9.1) than other histologies (OR 4.4), as well as the duration and magnitude of smoking relative to non-smokers. Relative to never-smokers, those smoking less than 20 cigarettes/day had a relative risk of 5.4, while those who had smoked for 20 years or more had a relative risk of 7.6. A higher risk (OR 16.5) was observed among smokers who had smoked for more than 40 years.[5,112,113]

**Nutrition**

A diet rich in vitamin A and carotenoids has been associated with a decreased risk of bladder cancer.

### *3.11.2 Infections*

There is a strong association between bladder cancer and infection with urinary schistosomiasis, based on evidence from clinical series, correlation studies, and case-control studies[5]. Most of the evidence is based on the larger proportion of SCC occurring concurrently with the presence of Schistosomiasis infection and the younger age (average 44 years) at diagnosis with bladder cancer. ORs of 15 (95% CI: 2.0, 114) and 6.5 (95% CI: 1.5, 29) (not adjusted for confounding factors) have been reported in Zimbabwe. After adjusting for confounders, including tobacco smoking, age, province of origin, education and occupation, relative risks of 3.9 (95% CI: 2.9, 5.2) and 5.7 (95% CI: 3.7, 8.7) were reported.[5,113]

### *3.11.3 Occupation*

Some other known risk factors for bladder cancer, which have not been investigated in Africa, are related to occupation. These include rubber and dyestuff industries, exposure to aromatic amines, polychlorinated biphenyls, polycyclic aromatic hydrocarbons, formaldehyde, asbestos, leather manufacturers, and painters.[5]

### *3.11.4 Genetic factors*

Several studies have demonstrated an increased risk of bladder cancer associated with glutathione S-transferase 1 (*GSTM1*) polymorphism. *GSTM1* is involved in conjugation of reactive chemicals such as nitrosamines. The relative risk associated with the null genotype of *GSTM1* ranges between 2.99 (95% CI: 1.0, 9.0) and 6.97 (95% CI: 1.34, 45.69).[114,115]

## 3.12 Stomach cancer

Stomach cancer was the most common cause of cancer mortality worldwide in 1980, but incidence and mortality has declined dramatically in recent years.[116] Stomach cancer is now about the fourth most common cancer in the world, with high incidence rates reported in Japan. However, incidence is lower in Africa possibly because of the rapid fatality rate and poor diagnosis of this cancer.

In South Africa in 1999, stomach cancer ranked sixth in males accounting for 2.6% of all male cancers reported to the NCR. The ASR has remained constant over time at about 6.0/100 000 in males. The risk of developing stomach cancer in males was three times that in females. The incidence of stomach cancer was highest among coloured males (ASR 16.3) where it ranked third, followed by Asian males (ASR 12.8) where it ranked fourth. African males and females had the lowest rates.[19]

The age-standardised death rate was also highest in coloured males (27.0) followed by Asian (23.7), white (17.3) and African (7.4) males. Stomach cancer death rates were high in coloured and Asian females (13.6 and 13.8, respectively) and lower in white and African females.

Incidence rates for stomach cancer are higher in developing countries with particularly high rates reported in Brazil and Mali.[111] In Mali, incidence rates for stomach cancer (17.3 in males) were more than three times higher than the overall rates in South African males in 1999. Rates in African females in Harare, Zimbabwe, (10.3) were more than 9 times the rates reported for African females by the NCR (1.4). The very low rates in the South African population are probably a result of underreporting. Incidence rates in Asian females in South Africa, however, were almost three times the rates reported for Indian females in Bombay.

### *3.12.1 Infections*

Several studies have shown that infection with the bacteria *Helicobacter pylori* is one of the main risk factors for the development of stomach cancer. Infection with this organism causes chronic active gastritis, eventually leading to chronic atrophic gastritis, a key precursor of stomach cancer.[116] Infection rates as high as 80% have been reported in South Africa; however, it is important to note that most infected people will remain asymptomatic and will not develop gastric cancer. Conversely, gastric cancer can occur in the absence of *H. pylori*.

### *3.12.2 Lifestyle factors*

An increased risk for this cancer has been associated with the consumption of smoked, pickled, and preserved foods. Low fruit and vegetable intake is another important risk factor, with about 24% of stomach cancer burden attributed to this (Table 12.4). High intake of antioxidants and refrigeration of food are protective factors. Decreasing infection with *H. pylori*, improvements in diet and domestic refrigeration have been responsible for the decreasing incidence of this cancer worldwide, but high salt intake, alcohol consumption and smoking remain important causes of stomach cancer.[116]

## 3.13 Melanoma

Melanoma is the third most common skin cancer worldwide after BCC and SCC of the skin. Melanoma comprised 2.6% of all male cancers in South Africa during 1998 to 1999. South African males had an ASR of 5.6/100 000 in 1999, with a lifetime risk of 1 in 150 of developing melanoma. Males had a 52% greater risk of developing melanoma than females. Melanoma comprised 2.4% of all the cancers reported in females, with an ASR of 4.2.[19]

Melanoma was more prevalent among white males comprising about three-quarters and females about two-thirds of all melanoma cases over the period 1998-1999. In 1999, melanoma was the third and fourth leading cancer in white females and males, respectively. The ASR was highest in white males (20.9), with a lifetime risk of 1 in 43, which is 16 times greater than the risk in African males. Rates were also highest in white females, with an ASR of 16.7.

Melanoma incidence rates in white South Africans are among the highest in the world, second only to Tasmania where rates as high as 27 and 28.7 in females and males, respectively, have been reported.[111]

Melanoma, as a cause of cancer deaths, ranked 19$^{th}$, accounting for 1% of all cancer deaths in South Africa 2000 (Table 12.1). Age-standardised death rates were highest in white males (6.6) and females (4.8) and very low in all other population groups.

### *3.13.1 Lifestyle factors*

The major risk factors for melanoma are exposure to the sun, a fair skin, and naevi (freckles). Ethnic origin and climate play important roles. Early age at first exposure to sunlight in fair-skinned population groups, as well as cumulative sun damage, are important risk factors.[5]

## 3.14 HIV/AIDS and cancer

Clusters of Kaposi's sarcoma (KS) emerging in the United States among homosexual males in conjunction with *Pneumocystis carinii* pneumonia in the late 1970s led to the discovery of acquired immune deficiency syndrome (AIDS) by the US Center for Disease Control.[21] There is little evidence, however, that the human immunodeficiency virus (HIV) plays a direct oncogenic role in the development of cancer. HIV is rather thought to promote the development of cancer through its effect on the immune system.[94]

Despite the high prevalence of HIV infection in South Africa, information on its association with cancer is sparse. A recent study examined the relationship between HIV and some common cancers in South Africa. In the control group, the prevalence of HIV infection was 8.3% in males and 9.1% in females. Significant excess risks associated with HIV infection were found for KS (OR 21.9, 95% CI: 12.5, 38.6), non-Hodgkin lymphoma (OR 5.0, 95% CI: 2.7, 9.5), vulvar cancer (OR 4.8, 95% CI: 1.9, 12.2) and cervical cancer (OR 1.6, 95% CI: 1.1, 2.3), but not for any of the other major cancer types examined, including Hodgkin's disease, multiple myeloma and lung cancer. The relative risks for KS and non-Hodgkin lymphoma associated with HIV infection were substantially lower than those found in Western countries.[117]

## 3.15 Kaposi's sarcoma

### *3.15.1 Descriptive epidemiology*

Before the onset of HIV/AIDS, KS was endemic in parts of sub-Saharan Africa, such as Uganda and the Democratic Republic of Congo, comprising about 9% of cancers in males. KS occurred to a lesser extent in South Africa and was very rare in other parts of the world. With the HIV/AIDS epidemic, KS has become the leading cancer in African countries with high HIV prevalence. Endemic KS affects predominantly the skin of the lower limbs and is primarily a disease of the elderly. In the epidemic form of KS, the lesions are usually multiple and may affect any area of the skin as well as internal organs, with incidence peaks also in the younger, sexually active age groups.

In Zimbabwe and Uganda, the incidence of KS has increased 20-fold in recent years and is now the most common cancer in males and the second most common cancer in females.[5,76] Incidence rates for African males in Harare, Zimbabwe, increased from 31.3 in 1990-1993 to 50.9/100 000 for the period 1994-1997.[5] The second highest incidence rates in males occurred in Malawi (49.9), where data that are more recent are available for 2000-2001, followed by Uganda (37.7) for 1993-1997. In females, the highest incidence rates were reported for Malawi (31.7 in 2000-2001), followed by African Zimbabweans (21.6 in 1994-1997).

In South Africa, a three-fold increase in the number of cases occurred between 1993 and 1995,[32] and a 62% increase was observed between 1996 and 1997. The lifetime risk increased from 1 in 1001 in 1996 to 1 in 496 in 1999. This is in keeping with the increases seen in Uganda and other central African countries at the beginning of the HIV epidemic.[5] In Uganda, KS alone caused a 15% increase in cancer incidence. An increase in the incidence of KS in South Africa has been noted in previous NCR reports,[94,32] and this incidence, although low, continues to rise. In a recent report from a hospital in rural KZN, KS was one of the leading cancers.[118] Incidence rates for KS depend on and reflect clinical practice and the extent to which affected individuals are biopsied and their specimens sent to laboratories, since these are the only source of registry data in South Africa.[19] More recent incidence data are needed to monitor trends.

The ASR of KS was 2.2 for all males and 1.2 for all females in 1999.[19] Africans constituted more than 90% of all cases reported. Among African males KS ranked 13$^{th}$ in 1998, comprising 3.4% of all cancer cases, while in 1999 it ranked seventh, comprising 4.4% of all cancers. A bimodal pattern in the age-specific incidence rate was observed with a first peak at young ages (35-39 in males and 25-29 in females) and a second peak in the older 70-74-year age group. Rates in African males increased from 1.8 in 1997 to 2.8 in 1999, with a lifetime risk of 1 in 385. In African females the ASR was 1.5, with a lifetime risk of 1 in 834. Rates were much lower in the other population groups.

### *3.15.2 Infections*

**HIV**

The close association between KS and immune suppression (whether post-transplant, because of cancer chemotherapy or HIV-induced) suggests that KS is under tight immunological control.[5,119] Two case-control studies in Johannesburg found elevated risks between HIV infection and the development of KS (see section 3.14 HIV/AIDS and cancer).[117,120]

**Human Herpes virus 8**

Human herpes virus 8 (HHV-8) has been causally linked to the development of KS,[121,122] but its mode of transmission, association with other cancers, and interaction with the human immunodeficiency virus type 1 (HIV-1) is largely unknown. HHV-8 infection in immunocompetent individuals is usually asymptomatic, however, KS occurs frequently in immunodeficient individuals, particularly patients with HIV/AIDS,[123] as well as immunosuppressed transplant recipients.[124]

Seroprevalence to HHV-8 varies worldwide. Prevalence is lowest in Asia, the United States, and Western Europe, higher in Southern European and Middle Eastern Mediterranean populations, and highest in Africa, where KS was endemic pre-HIV/AIDS. In South Africa, 35% of rural,[125] and about 30% of urban[126] African adult hospital patients were found to be HHV-8 seropositive. HHV-8 antibodies were more frequent among African compared with white blood donors (P <0.001).[126]

In a study among African patients with cancer who were interviewed in Johannesburg and Soweto,[126] the authors found the seroprevalence of anti-HHV-8 antibodies to be high and specifically associated with KS, particularly at high titres. Among the 3 293 patients with cancers other than KS, the standardised seroprevalence of antibodies against HHV-8 did not differ significantly from the standardised seroprevalence among African blood donors. The prevalence of antibodies against HHV-8 increased with increasing age (P <0.001) and an increasing number of sexual partners (P = 0.05), and decreased with increasing years of education (P = 0.007). HIV-1 infection did not appear to have an effect on the presence of anti-HHV-8 antibodies. Prevalence of antibody to HHV-8 was 30% in HIV seropositive and 33% in seronegative subjects.[126] This suggests that the effect of the two viruses on risk is independent (and more or less multiplicative) in the causation of KS. The effect of HIV is probably through immunosuppression, by allowing HHV-8 to escape control and increase viral load.[5]

KS was the only cancer among the 17 types studied that was associated with a high seroprevalence of antibodies against HHV-8. Among the 51 patients with KS, the standardised seroprevalence of antibodies against HHV-8 was 83%, which was significantly higher than the prevalence among those without KS (P <0.001). For the other specific types of cancer, including multiple myeloma (108 cases) and prostate cancer (202 cases), the variation in the standardised seroprevalence of antibodies against HHV-8 was not statistically significant. At a given intensity of fluorescence of anti-HHV-8 antibodies, KS was more frequent among HIV-1-positive patients than among those who were HIV-1-negative (P <0.001).[126]

In Africa, sexual transmission of HHV-8 is important in adolescents and young adults. Vertical (mother-to-child) transmission does not appear to occur. Antibodies to HHV-8 are transmitted transplacentally so that most children born to seropositive mothers have antibodies present at birth, but titres drop rapidly thereafter. HHV-8 seropositive mothers with high antibody titres are about twice as likely to have HHV-8 seropositive children, as mothers with low titres, suggesting some form of person-to-person transmission may be at play.

Other non-sexual routes of transmission are also important.[126] Risk factors for HHV-8 include birth in a rural area and a low standard of education, suggesting that factors related to poverty may contribute to transmission of the virus. The age (or the route of infection) at which infection occurs could affect the subsequent risk of KS.[126]

## 3.16 Cervical cancer

### *3.16.1 Descriptive epidemiology*

Cancer of the cervix is the second most common cancer in women worldwide, and the leading female cancer in the developing world.[96,98] Cancer of the cervix was declared an AIDS-defining condition in 1993. In Africa, where there is high incidence of both cervical cancer and HIV infection, there is good data showing an increased incidence of invasive cervical cancer with the HIV epidemic. Since 1960, a moderate increase in cervical cancer was reported for all age groups in Uganda.[111] Data from the NCR[19] on cervical cancer have so far not shown any significant increases in cervical cancer, especially in younger age groups that are more susceptible to HIV infection. HIV prevalence has increased since 1999, and data from the NCR that are more recent would be important to determine whether there is an increase in cervical cancer incidence rates in these young at-risk age groups. However, underreporting in vulnerable groups remains a problem.

In South Africa, cervical cancer had consistently been the leading cancer in females in terms of incidence and death. In 2000, cervical cancer was still the leading cause of cancer deaths in women, accounting for 17.2% of all female cancer deaths. However, of all cancer cases reported in 1999, cervical cancer was the second leading cancer after breast cancer in terms of incidence in females, accounting for 17%.[19]

Age-standardised incidence rates for all females dropped from 34.4 in 1998 to 29.7/100 000 in 1999, with a lifetime risk of one in 30 (age range 0-74 years), while the age-standardised mortality rate for females in South Africa, was estimated at 20.8 in 2000. In Australia, the ASR is 3.3-fold higher than the age-standardised death rate,[92] while in South Africa it is only 1.4-fold higher. This could be because of minimal incidence rates being reported by the NCR, especially in the African population, or to higher mortality from this cancer in South African females.

African females comprised about 84% (4127) of all cervical cancer cases reported to the NCR in 1999, with a lifetime risk of one in 25. The risk of developing this cancer was more than three times higher in African females than in white and Asian females.[19]

Cervical cancer was the second most common cancer in females (second to oesophageal cancer) reported to the PROMEC Registry for 1996-2000, with an overall ASR of 15.2. The highest incidence rate was reported in Lusikisiki (27.2), followed by Butterworth (21.9), with Bizana (13.4) and Centane (13.5) having very similar rates. Incidence rates in Butterworth increased three-fold in 1996-2000 compared with the 1991-1995 data.[23]

Age-standardised death rates for cervical cancer were also highest in African females (26.9), followed by coloured females (21.7). White and Asian females had relatively low rates (5.5 and 7.6, respectively). The risk of developing this cancer increased with age with the ASR peaking at 136.4 at age 65-69 in 1999. Similarly, in Fig. 7, the age-specific death rates clearly indicate a steady rise in mortality rate from the young age groups (25-34 years) in coloured and African females (this pattern is not so clear for Asian females, possibly because of small numbers in the older age groups). Limpopo and Mpumalanga provinces had the highest age-standardised mortality rates of cervical cancer (Figs. 8 and 9).

Despite the minimum rates reported by the NCR, cervical cancer incidence rates in South Africa are among the highest in the world. In 1999, incidence rates in African females in South Africa (34.9 in 1999) were the fourth highest in Africa, with the highest rates reported for African females in Zimbabwe (53.1 in 1994-1997) and Malawi (53.1 in 2000-2001), followed by Kyadondo, Uganda (40.7 1993-1997).[5,21,111] The incidence rate of cancer of the cervix in African females was also similar to rates observed in the New Zealand Maori population (32.2 ).[92]

### *3.16.2 Infections*

**Human Papilloma Virus**

Infection with HPV is now recognised as the main aetiological factor for invasive and pre-invasive cervical neoplasia worldwide. Persistent infection with high-risk oncogenic HPV types (including types 16, 18, 31, 33, 39, 45, 52 and 58) is known to be a necessary cause of cervical cancer.[127-132] The worldwide prevalence of HPV in cervical carcinomas is reported to be 99.7%.[128]

**HIV/AIDS**

Although a slight association between HIV and cancer of the cervix (OR 1.6, 95% CI: 1.1, 2.3) was found in the case-control study in Johannesburg,[117] a former study appeared to contradict this finding.[133] Nevertheless, a similar relative risk was noted in Uganda[134] (OR 1.6), and in Rwanda.[135,136] Other studies have demonstrated an association between HIV and the increased prevalence of HPV and cervical intraepithelial neoplasia (CIN).[134,137] In an outpatient clinic in Senegal, a three-fold (OR 3.3, 95% CI: 0.9, 12.4) and eight-fold, (OR 7.9, 95% CI: 1.1, 57) increased risk of high grade cervical squamous intraepithelial lesions and invasive cervical cancer, respectively, has been reported in females infected with high-risk HPV and HIV-2 compared to those infected with HPV and HIV1.[138]

### *3.16.3 Reproductive factors and sexual behaviour*

Some endogenous or exogenous factors are believed to act in conjunction with HPV infection to cause invasive cancer. Other risk factors known to be strongly associated with invasive cervical cancer include low social class and reproductive factors and sexual behaviour, such as the lifetime number of sexual partners and early age at first intercourse.[139] Two studies reported an increased risk of developing both squamous cell and adenocarcinomas with increasing duration of use of oral contraceptives.[127,140] A systematic review of 28 published studies examined the relationship between invasive and *in situ* cervical cancer and duration of hormonal contraceptive use, with particular attention to HPV infection; durations of 5-9 years and 10 years or more were associated with a significantly increased risk of developing the cancer (RR 1.6, 95% CI: 1.4, 1.7) and (RR 2.2, 95% CI: 1.9, 2.4), respectively, in all females.[141] For the same durations, RRs of 1.3 (95%

CI: 1.0, 1.9) and 2.5 (95% CI: 1.6, 3.9) were reported for HPV-positive females. Evidence of the relationship between progestogen only contraceptives and cervical cancer is, however, unclear. Furthermore, no evidence has been reported of a strong positive or negative association between HPV-positivity and ever use or long duration of oral contraceptives.[140] The risk of developing squamous cell cervical cancer is associated with high parity and both squamous and adenorcarcinoma cervical cancers increase with early age at first birth.[139]

### 3.16.4 Lifestyle factors

**Tobacco smoking**

A two-fold increase in risk of developing squamous cell cervical cancer in those who had been smoking for over 20 years, compared to non-smokers, has been reported.[139] Excess risk for cervical cancer among smokers has been observed in a number of studies even after controlling for other potential confounding factors, such as reproductive factors and infection with HPV.[142]

# 4 CANCER PREVENTION EFFORTS AND RECOMMENDATIONS

## 4.1Cancer control programmes

Cancer is a major public health problem in South Africa, with several social and economic implications. Job loss, economic dependence, social isolation and family tensions often follow the occurrence of cancer.[143] There are direct health-care costs from hospital admissions, drugs and health professional services, as well as indirect costs associated with disruption of productivity by disability and premature mortality.[23] As South Africa undergoes development, the current risk profile will translate into increasing rates of cancer, unless policies are formulated and implemented to ameliorate the detrimental effects of the key risk and lifestyle factors. Implementation of a well co-ordinated and comprehensive cancer prevention and control programme is crucial if activities that contribute to risk reduction efforts are to be successful.[19] About one third of new cancer cases diagnosed every year are preventable by controlling tobacco and alcohol use, moderating diet and immunising against certain viruses. With early detection and treatment, reduction of a further one third is possible.[144]

### 4.1.1 Primary and secondary prevention

Prevention means eliminating or reducing exposure to known risk factors or cancer-causing agents. The most common approach to cancer prevention is health education or health promotion to empower people with information to change unhealthy lifestyles (primary prevention). Another approach is early detection or screening of seemingly healthy individuals to detect cancer in its early or precursor stages when treatment will be most effective (secondary prevention).

The South African government has put in place new legislation and policies as an effort to reduce cancer. These include the Tobacco Products Control Amendment Act of 1999,[145] the Cervical Screening Programme Policy,[146] and, following the WHO recommendations, immunisation against hepatitis B to prevent liver cancer. To sustain the public health advances that have already been achieved, cancer needs to be dealt with appropriately. Effective implementation of these programmes will go a long way in reducing these cancers. Close monitoring and evaluation of these intervention programmes is therefore essential to measure and ensure successful and cost-effective implementation.

In addition, reducing the transmission of HIV and delaying mortality from AIDS will also play an important role in reducing the dramatic increase in incidence of cancers related to HIV/AIDS. This could be done by improving the treatment of sexually transmitted infections, improving the voluntary counselling and testing services, and providing antiretroviral treatment to pregnant and other HIV-positive persons, and health education in promoting safe sex. A comprehensive HIV and AIDS Care, Management and Treatment Programme[147] for South Africa is currently being implemented and monitored, and efforts to curb the HIV/AIDS epidemic will have a positive impact on cancer of the cervix. Strengthening health promotion efforts aimed at the youth (including safer sex, gender violence, smoking and alcohol abuse) and promoting healthy lifestyles (including diet, physical activity, and reducing alcohol and substance abuse) are important strategies likely to reduce the burden of cancer in South Africa.

### 4.1.2 Tobacco control legislation

Recent years have seen the introduction of tobacco control legislation including severe restrictions on advertising, health warnings on tobacco products and the banning of smoking in public places. In addition, excise taxes for tobacco products have been increased, and between 1994 and 1999, real excise taxes on cigarettes went up by 149%. These taxes have been extremely powerful in reducing cigarette consumption. Figures from the South African National Council Against Smoking indicate that legal sales of commercial cigarettes have fallen every year since peaking at 40 billion in 1990.[148] Therefore, it can be optimistically expected that South Africa is past the peak of its tobacco consumption epidemic, and that tobacco-related cancers will begin to decline in time.[38]

In contrast, little effort has been made to curb alcohol abuse. Total adult per capita pure alcohol consumption was estimated to be 10 ℓ in 1995 and 12 ℓ in 2000, and has increased by over 50% since 1970.[149]

### *4.1.3 Cervical cancer screening*

The high mortality burden caused by cervical cancer among the poor indicates an inadequacy in the provision of primary care to these communities. Therefore, it is essential to ensure that females in poor areas are screened for cervical cancer so that this mortality can be reduced.

Trends in cervical cancer incidence rates have been significantly reduced in countries where effective cervical cancer screening programmes were implemented, particularly in developed countries.[98] In New South Wales (NSW), Australia, both age-standardised incidence and mortality rates fell by about 40% over the period 1991 to 2001, mainly because of the introduction of population screening. In 2001, 60% of all NSW females aged 20-69 years were screened for cervical cancer every two years.[92]

The South African cervical cancer screening policy and the cervical cancer-screening programme that have been implemented since 2001, aim to reduce the incidence of this disease.[146,150] This is done primarily by detecting and treating the pre-invasive stage and reducing the morbidity and mortality associated with the cancer. Ultimately, this will reduce the excessive expenditure of limited health funds that are currently being spent on the treatment of invasive cancer of the cervix. Three free smears per lifetime are recommended for the programme, commencing after age 30 years and with a 10-year interval between each smear. The ultimate goal is to reduce the incidence of cervical cancer by 60%.[150] However, there are concerns that this programme has not been implemented uniformly across the country.

The programme has not yet been put into practice in primary and secondary health centres in the former Transkei region of the Eastern Cape, because of shortage of staff and equipment. According to Somdyala *et al.*,[23] capacity development to improve skills and efficiency of health professionals is an essential first step. Provision of basic equipment for pap smears at all clinics, followed by provision of relevant follow-up facilities, and specialists for cases that require further investigations are also essential. A screening evaluation programme should also be established with links to cancer registries. Most importantly, females need to be informed of the importance of this programme.

In low-resourced countries that are faced with challenges, such as few laboratories or cervical cytology of poor quality, efforts are being made to develop other accurate and affordable tests to pick up cervical cancer at an early stage. A new technique, the visual inspection of the cervix following acetic acid staining (VIA), is being investigated, and it could be conducted by specially trained health workers. A review of studies conducted on VIA between 1982 and 2002 suggested, "VIA has the potential to be a cervical cancer screening tool, especially in low resource settings."[151]

Other approaches that are currently underway in an effort to control cancer of the cervix include the development of HPV DNA screening tests and HPV vaccines to help control the infection. In a study of 2 944 cervical samples from South African females, Kuhn *et al.*[152] concluded that HPV DNA testing programmes might be easier to implement than cytological screening, and that this approach should be considered for screening in low-resource settings. The WHO, however, considers that the test requires sophisticated technical resources and is therefore not yet ready for routine application with a national cancer control programme.

### *4.1.4 Treatment*

The objectives of treatment are to cure, control symptoms, prolong useful life, and improve the quality of cancer survival. In South Africa, cancer treatment is often centralised at the main referral hospitals, meaning that patients in rural areas have to travel long distances to reach treatment facilities. This has negative physical and emotional effects resulting in low compliance to treatment. A better cancer management programme may improve compliance.[23]

## 4.2 THE CANCER ASSOCIATION OF SOUTH AFRICA

Hospices and organisations, such as the Cancer Association of South Africa (CANSA), can play an important role in the community. Counselling and support programmes help cancer patients and relatives come to terms with the illness. However, provision of support programmes is still needed in many rural areas.

CANSA is a registered non-profit organisation founded in 1931 by a group of volunteer doctors concerned about the incidence of cancer in the country. The organisation has since grown throughout the country and provides a range of services from education, prevention and advocacy work, to facilitating research, treatment, and care and support for cancer patients, survivors and their families.[153] CANSA relies on private and corporate donors as well as its own fundraising initiatives.

Historically, CANSA support was mainly for biomedical cancer research, but since 2003 it has remodelled its programmes to increase focus on health promotion and advocacy. Their research support is also geared towards informing public health, interventions, programmes and advocacy.

## 4.3 CANCER SURVEILLANCE

Globally, cancer surveillance plays an important role in informing the development of cancer control programmes and monitoring their success.[154] Data from the better-performing cancer surveillance programmes, by means of recommended population-based cancer registries, have been published in the WHO series of *Cancer incidence in five continents*.[5] The picture emerging from this work shows many gaps in our knowledge about the burden of cancer in Africa. Scientific forums around cancer and cancer management have expressed a need for cancer registries in Africa to do more than to report cancer incidence.

One of the recommendations of the National Cancer Control Programme (NCCP)[155] was that data on cancer registry incidence and cancer mortality should form the basis of monitoring and evaluating the progress in cancer control in South Africa. The importance of cancer surveillance in monitoring the extent of the increase in cancer incidence caused by HIV/AIDS is important. Accurate information on cancer incidence, prevalence and mortality, however, is essential for this process and further research is required to improve national cancer mortality and incidence estimates.

One of the challenges of the SA NBD study was the lack of recent complete and reliable mortality data. The study grappled with the inadequacies of the vital statistics, and had to use multiple sources of information to derive coherent and consistent estimates for the level and causes of mortality for the year 2000. As data that are more recent became available, these initial estimates were revised and improved.[16] Unfortunately, at this stage, estimates of years lived with disability (YLDs) and cancer disability adjusted life years (DALYs) for South Africa are still based on extrapolations from the global burden of disease study.[156] Accurate national incidence data, as well as information on the severity and the duration of the disease, are essential in order to improve estimates of the extent of the cancer burden. These data can be used as a benchmark to monitor change and for identifying priorities.

In the absence of any legislative framework of disease reporting, pathology laboratories around the country have voluntarily sent data to the NCR since its inception. This ongoing national collaboration across private and public sectors is remarkable.[19] Demographic data and tumour information are sent to the NCR for each cancer patient. Ethical guidelines are being developed to receive and hold this confidential information in keeping with concerns on privacy. Nevertheless, incomplete submission of data remains one of the limitations of this voluntary and passive surveillance system, with accurate incidence rates depending on the quality of data submitted to the NCR. Pathology laboratories should insist that basic demographic details of patients are properly completed. This would greatly enhance the epidemiological value of the data.

The incidence rates reported by the NCR are minimal rates and could be improved with the implementation of a more comprehensive data collection system, such as a population-based cancer registry. Such registries record information from all sources (pathology, mortality reports and clinical information). The establishment of population-based cancer registries in each of the nine provinces is regarded as one of the essential components of the Department of Health's NCCP. However, trained personnel and adequate funding are essential to ensure the long-term sustainability of these registries.[19] Increased efforts should concentrate on establishing comprehensive co-operative regional registration systems. Collaboration of regional registries and pooled analysis of data to reflect national trends has been followed successfully in several countries.[19] Another strategy to improve cancer incidence estimates would be that cancer becomes a reportable condition by law.

Monitoring cancers by population group would enable the NCR to further extend and evaluate the effectiveness and equity of access of the cervical cancer and tobacco control policies. Monitoring disease across different population groups is critical to measure the equity of efforts in different parts of the country, as well as that of health outcomes in the different groups. However, about two-thirds of the collected data in 1998, and three-quarters in 1999, did not report on the population group of cases, making it difficult to discern important cancer incidence patterns by population group.

South African "racial" terminology devised by previous Apartheid legislators was unscientific and often used without justification in medical research. However, because of this classification, different population groups have been subjected to environments that have played an important role in determining their lifestyle, socio-economic condition, residence and access to health care. These differences have played an important role in the cancer patterns observed in different population groups. NCR data are therefore analysed by population group as a proxy of a combination of dietary, lifestyle and socio-demographic factors to provide clues about cancer aetiology. It appears to be the only viable option in discerning important epidemiological sub-groups and access to health care - both vital indicators of the performance of the health system.[32]

## 4.4 CANCER RESEARCH INITIATIVE OF SOUTH AFRICA

The important CANSA/MRC workshop held in February 2004 evaluated the future of cancer research in the country and resulted in a proposal for the creation of a multi-disciplinary, multi-organisational group called the Cancer Research Initiative of South Africa (CRISA). The initiative suggested combined efforts of the two organisations to promote and expand cancer research. Administrators and cancer researchers met to discuss the way forward for effective cancer research in South Africa, and a joint research initiative was developed to co-ordinate, focus and extend existing cancer research appropriately.

CRISA aims to improve the health status of South Africans by promoting a national, comprehensive and sustainable cancer research system that will develop capacity and knowledge in the following areas: primary prevention, secondary prevention, treatment, palliation, and monitoring and evaluation.

Scientific research that includes aetiological and epidemiological studies should generate flagship projects, which will add value to advocacy strategies that are aimed at influencing policy development and intervention programmes at government, private and public levels.[157] Some of the outcomes of the discussions included a rapid assessment and prioritisation of the key strategic issues, a synopsis of current research (presented in a matrix form based on process and cancer type in Table 12.6), an environmental analysis, and the development of a proposed research structure together with its draft mission statement. CRISA progress will be driven by its Steering Committee.

Table 12.6. Integrated cancer research matrix (Adapted from Albrecht[157])

| | Breast | Cervix | Prostate | Lung | Colorectal | Oesophageal | Liver | Kaposi's | Lymphoma | Mouth, oropharynx |
|---|---|---|---|---|---|---|---|---|---|---|
| Ranking as cause of cancer death | 4 | 3 | 7 | 1 | 6 | 2 | 5 | Not listed | 12 | 10 |
| Process: Primary Prevention | Genetic counselling | HPV vaccine | - | Anti-smoking | Genetic counselling | Health promotion | HBV Vaccine Anti-aflatoxin measures | Health promotion Safe sex | Health promotion Safe sex | Health promotion Anti-smoking |
| Secondary Prevention | - | PAP smear | PSA | - | - | Brush biopsy | - | - | - | Screening by Dentists |
| Treatment | Clinical Trials Drug discovery | Smit Tube Drug discovery | Drug discovery Hormone trials. Distinction between aggressive, non-aggressive types of surgery | Drug discovery | Drug discovery | Drug discovery Radiation schedules | Drug discovery Radiation schedules | Drug discovery Radiation schedules | Drug discovery Radiation schedules | Drug discovery Radiation schedules |
| Palliation | - | Search for cost-effective schedules | - | - | - | - | - | - | - | - |
| Burden of disease | + | + | + | + | + | + | + | + | + | + |
| Advocacy | - | - | - | - | - | - | - | - | - | - |
| Audit | - | Bloch study Only 20% have had Pap smear | - | - | - | - | Peanut butter incident in children | | | |

+ Incidence data from NCR, mortality data from MRC Burden of Disease Research Unit

- Research gap

## 5 CONCLUSIONS

Cancer is not only a major public health problem but also has widespread social and economic impacts. Changing lifestyles, particularly among the African population, combined with population ageing and the increasing prevalence of HIV have placed South Africans at greater risk of developing cancer.

Promoting healthy lifestyles (including diet, physical activity, reducing smoking, alcohol, and substance abuse) is an important strategy to reduce the large burden of cancer in South Africa. The tobacco control intervention is having a demonstrable effect on tobacco consumption that will translate into reducing the future number of cancers. However, it is important for the programme to be monitored and maintained. In addition, promoting safe sex is essential in reducing the transmission of HIV and other sexually transmitted diseases, and along with improving the integrated management of childhood diseases and immunization, these remain clearly important strategies in South Africa.

Research on the causes of some of the most important cancers, including cancers of the oesophagus, cervix and skin, should be undertaken. Methods of reducing exposure to the sunshine, including health promotion efforts, should also be investigated.

Monitoring cancer incidence and mortality is important in detecting changes in cancer patterns that might occur because of changes in environmental conditions and increases in cancers associated with new diseases. It also serves to detect new cancers and to measure the effectiveness of currently implemented cancer control programmes in our country. Monitoring the number of AIDS-related cancers, especially KS and non-Hodgkin's lymphoma, should be a priority. Another priority is monitoring the prevalence of tobacco use and the tobacco-attributable burden of cancer. With appropriate resources, cancer registries would be able to meet these challenges.

Close monitoring and control of cancer of the cervix is essential, and it is hoped that long-term, effective implementation of cervical cancer screening programmes and early intervention will reduce its high incidence and mortality. The need for screening for oesophageal cancer in poor areas of high risk should also be investigated. Breast cancer incidence is high and appears to be increasing, and the cost-effectiveness of a screening programme for women over 50 years[158] should be analysed.

The magnitude of cancer as a health problem is estimated from limited sources. The voluntary and limited nature of data reporting to the NCR affects the timeliness and completeness of reporting of cancer incidence data. A pathology-based registry remains a problem when a large proportion of the population, mainly rural African, has limited access to diagnostic facilities. Despite these limitations, most of the cancer policy guidelines are based on NCR data. Re-establishment of population-based cancer registries and making cancer a reportable condition are recommended to improve the quality and accuracy of the national cancer incidence data.

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